

Ozga 09/775,517

=> d.his  
(FILE 'REGISTRY' ENTERED AT 11:49:36 ON 18 OCT 2001)  
DEL HIS Y  
1 S LYSOSMAL ACID LIPASE/CN

L1 FILE 'HCAPLUS' ENTERED AT 11:50:40 ON 18 OCT 2001  
1745 S L1 OR LYSOSMAL ACID LIPASE OR ESTERASE (2A) CHOLESTEROL  
L2 0 S LIPID HYDROLYAING (L) (PROTEIN# OR POLYPEPTIDE#)  
L3 0 S LIPID HYDROLYZING (L) (PROTEIN# OR POLYPEPTIDE#)  
L4 0 S LIPID(L) HYDROLYZING (L) (PROTEIN# OR POLYPEPTIDE#)  
L5 11 S LIPID(L) HYDROLYZING (L) ENZYME?  
L6 1754 S L2 OR L6  
L7 36 S TARGET? (L) RECEPTOR (L) LYSOSOME?  
L8 1 S L7 AND L8  
L9 1486 S MANNOSE (L) RECEPTOR?  
L10 6 S L7 AND L10  
L11 22055 S ATHEROSCLEROSIS? OR ANTIARTERIOSCELER?  
L12 24524 S ATHEROSCLEROSIS? OR ANTIARTERIOSCELER?  
L13 24524 S L13 OR ANTIATHERIOSCELER?  
L14 25226 S L13 OR ANTIATHEROSCELER?  
L15 128 S L15 AND L7  
L16 1 S L16 AND MANNOSE?  
L17 46481 S VECTOR?  
L18 1 S L16 AND L18  
L19 15431 S ACETYLGLYCOSYL? OR LYSOSOME?  
L20 25 S L20 AND L16  
L21 6 S L9 OR L11 OR L17 OR L19  
L22 69164 S GENE THERAPY OR DRUG DELIVER?  
L23 2 S L16 AND L23  
L24 123743 S MUTAT?  
L25 128 S L16 AND L2  
L26 3 S L16 AND L25  
L27 243 S WOLMAN? OR CHOLESTER? (2A) STORAGE?  
L28 4 S L28 AND L16  
L29 470344 S DISEAS? OR DISORDER?  
L30 21 S L30 AND L16  
L31 21 S L30 AND L16  
L32 794880 S TREA? OR THERAP?  
L33 4 S L31 AND L32  
L34 14 S L22 OR L24 OR L27 OR L29 OR L33  
L35 14 S L31 NOT L34

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=> fidl reg  
FIDL IS NOT A RECOGNIZED COMMAND

=> fil reg  
FILE 'REGISTRY' ENTERED AT 12:03:53 ON 18 OCT 2001  
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STRUCTURE FILE UPDATES: 16 OCT 2001 HIGHEST RN 362587-51-7  
DICTIONARY FILE UPDATES: 16 OCT 2001 HIGHEST RN 362587-51-7

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER see  
HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d que l1;d l1  
L1 1 SEA FILE=REGISTRY ABB=ON LYSOSOMAL ACID LIPASE/CN

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS  
RN 9026-00-0 REGISTRY  
CN Esterase, cholesterol (9CI) (CA INDEX NAME)

OTHER NAMES:

CN Cholesterase  
CN Cholesterin esterase  
CN Cholesterol ester hydrolase  
CN Cholesterol esterase  
CN Cholesteryl ester hydrolase  
CN Cholesteryl esterase  
CN E.C. 3.1.1.13  
CN Lysosomal acid lipase  
CN Neutral cholesteryl ester hydrolase  
CN Sterol ester hydrolase  
CN Sterol esterase  
DR 9040-56-6  
MF Unspecified  
CI MAN  
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,  
CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, EMBASE,  
IFICDB, IFIPAT, IFIUDB, PROMT, TOXLIT, USPATFULL  
Other Sources: EINECS\*\*, TSCA\*\*  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
1576 REFERENCES IN FILE CA (1967 TO DATE)  
21 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
1580 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> fil hcplus

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FILE 'HCAPLUS' ENTERED AT 12:04:00 ON 18 OCT 2001  
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FILE COVERS 1947 - 18 Oct 2001 VOL 135 ISS 17  
FILE LAST UPDATED: 17 Oct 2001 (20011017/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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(FILE 'REGISTRY' ENTERED AT 11:49:36 ON 18 OCT 2001)

FILE 'HCAPLUS' ENTERED AT 11:50:40 ON 18 OCT 2001

L2	1745 S L1 OR LYSOSMAL ACID LIPASE OR ESTERASE (2A) CHOLESTEROL
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FILE 'REGISTRY' ENTERED AT 12:03:53 ON 18 OCT 2001

FILE 'HCAPLUS' ENTERED AT 12:04:00 ON 18 OCT 2001

=> d .ca 134 1-14;d ibib ab 135 1-14

L34 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 2001:581727' HCAPLUS  
 DOCUMENT NUMBER: 135:147445  
 TITLE: Use of lysosomal acid  
 lipase for treating  
 atherosclerosis and related diseases  
 INVENTOR(S): Grabowski, Gregory A.; Du, Hong  
 PATENT ASSIGNEE(S): Children's Hospital Research Foundation, USA  
 SOURCE: PCT Int. Appl., 61 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001056596	A1	20010809	WO 2001-US3841	20010202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			US 2000-180362	P 20000204

PRIORITY APPLN. INFO.:

AB The present invention comprises a method to diminish and/or eliminate atherosclerotic plaques, in mammals, through direct and indirect treatment of these plaques, *in situ*, using suitable substances which are capable of lipid removal, primarily through hydrolysis, either by a catalytic or stoichiometric process, wherein the substance targets receptors in and/or on the cell which lead to uptake into the lysosome. Such substances used to diminish and/or eliminate atherosclerotic plaques are generally comprised of lipid hydrolyzing proteins and/or polypeptides.

IC A61K038-46; A61K048-00; A61P009-10; A61P003-06

CC 1-10 (Pharmacology)

ST Section cross-reference(s): 63

lysosome acid lipase atherosclerosis treatment;

lipid hydrolyzing enzyme

atherosclerosis treatment

IT Enzyme functional sites  
 (N-linked acetylglycosylation residues; use of lysosomal

acid lipase for treating

atherosclerosis and related diseases by

targeting receptor site for uptake into

lysosomes)

IT Disease, animal  
 (Wolman's, treatment; use of lysosomal  
 acid lipase for treating

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atherosclerosis and related diseases by targeting receptor site for uptake into lysosomes)

IT Antiarteriosclerotics  
(antiatherosclerotics; use of lysosomal acid lipase for treating atherosclerosis and related diseases by targeting receptor site for uptake into lysosomes)

IT Drug delivery systems  
(controlled-release; use of lysosomal acid lipase for treating atherosclerosis and related diseases by targeting receptor site for uptake into lysosomes)

IT Adeno-associated virus  
Adenoviridae  
Lentivirus  
(in genetic vector for lipid-hydrolyzing enzyme; use of lysosomal acid lipase for treating atherosclerosis and related diseases by targeting receptor site for uptake into lysosomes)

IT Drug delivery systems  
(infusions, i.v.; use of lysosomal acid lipase for treating atherosclerosis and related diseases by targeting receptor site for uptake into lysosomes)

IT Drug delivery systems  
(inhalants; use of lysosomal acid lipase for treating atherosclerosis and related diseases by targeting receptor site for uptake into lysosomes)

IT Drug delivery systems  
(injections, i.p.; use of lysosomal acid lipase for treating atherosclerosis and related diseases by targeting receptor site for uptake into lysosomes)

IT Drug delivery systems  
(injections; use of lysosomal acid lipase for treating atherosclerosis and related diseases by targeting receptor site for uptake into lysosomes)

IT Drug delivery systems  
(lipid vesicles, for lipid-hydrolyzing enzyme gene therapy; use of lysosomal acid lipase for treating atherosclerosis and related diseases by targeting receptor site for uptake into lysosomes)

IT Genetic vectors  
Plasmid vectors  
Virus vectors  
(lipid-hydrolyzing enzyme-contg.; use of lysosomal acid lipase for treating atherosclerosis and related diseases by targeting receptor site for uptake into lysosomes)

IT Gene, animal  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(lipid-hydrolyzing enzyme-encoding; use of lysosomal acid lipase for

treating atherosclerosis and related diseases  
by targeting receptor site for uptake into  
lysosomes)

IT Enzymes, biological studies  
RL: BAC (Biological activity or effector, except adverse); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(lipid-hydrolyzing; use of lysosomal  
acid lipase for treating  
atherosclerosis and related diseases by  
targeting receptor site for uptake into  
lysosomes)

IT Gene, animal  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological  
process); THU (Therapeutic use); BIOL (Biological study); PROC (Process);  
USES (Uses)  
(lysosomal acid lipase-encoding; use of  
lysosomal acid lipase for treating  
atherosclerosis and related diseases by  
targeting receptor site for uptake into  
lysosomes)

IT Lipids, biological studies  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(metabolic disorders, cholestryl ester  
storage disease, treatment; use of  
lysosomal acid lipase for treating  
atherosclerosis and related diseases by  
targeting receptor site for uptake into  
lysosomes)

IT Gene therapy  
(of lipid-hydrolyzing enzyme; use of  
lysosomal acid lipase for treating  
atherosclerosis and related diseases by  
targeting receptor site for uptake into  
lysosomes)

IT Mutation  
(of lysosomal acid lipase; use of  
lysosomal acid lipase for treating  
atherosclerosis and related diseases by  
targeting receptor site for uptake into  
lysosomes)

IT Oligosaccharides, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(on lysosomal acid lipase, receptors for;  
use of lysosomal acid lipase for  
treating atherosclerosis and related diseases  
by targeting receptor site for uptake into  
lysosomes)

IT Drug delivery systems  
(oral; use of lysosomal acid lipase for  
treating atherosclerosis and related diseases  
by targeting receptor site for uptake into  
lysosomes)

IT Drug delivery systems  
(parenterals; use of lysosomal acid lipase  
for treating atherosclerosis and related  
diseases by targeting receptor site for  
uptake into lysosomes)

IT Peptides, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(receptors for; use of lysosomal acid  
lipase for treating atherosclerosis and  
related diseases by targeting receptor  
site for uptake into lysosomes)

IT Drug delivery systems

Lysosome  
(use of lysosomal acid lipase for  
treating atherosclerosis and related diseases  
by targeting receptor site for uptake into  
lysosomes)

IT Mannose receptors

Receptors  
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
(use of lysosomal acid lipase for  
treating atherosclerosis and related diseases  
by targeting receptor site for uptake into  
lysosomes)

IT 3458-28-4, Mannose

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(on lysosomal acid lipase,  
receptors for; use of lysosomal acid  
lipase for treating atherosclerosis and  
related diseases by targeting receptor  
site for uptake into lysosomes)

IT 9026-00-0, Lysosomal acid lipase

RL: BAC (Biological activity or effector, except adverse); THU  
(Therapeutic use); BIOL (Biological study); USES (Uses)  
(use of lysosomal acid lipase for  
treating atherosclerosis and related diseases  
by targeting receptor site for uptake into  
lysosomes)

REFERENCE COUNT:

6

REFERENCE(S):

- (1) Du, H; AM J HUMAN GENET 1995, V57, PA178
- (2) Du, H; HUMAN MOLECULAR GENETICS 1998, V7, P1347  
HCAPLUS
- (3) Escary; ARTERIOSCLER, THROMB, VASC BIOL 1998,  
V18(6), P991 HCAPLUS
- (4) Reader; FASEB J 1996, V10, PA233
- (5) Sheriff; J BIOL CHEM 1995, V270, P27766 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:411495 HCAPLUS

DOCUMENT NUMBER: 135:179631

TITLE: Profiling changes in gene expression during  
differentiation and maturation of monocyte-derived  
dendritic cells using both oligonucleotide microarrays  
and proteomics

AUTHOR(S): Le Naour, Francois; Hohenkirk, Lyndon; Groleau,  
Annabelle; Misek, David E.; Lescure, Pascal; Geiger,  
James D.; Hanash, Samir; Beretta, Laura

CORPORATE SOURCE: Department of Microbiology and Immunology, University  
of Michigan, Ann Arbor, MI, 48109-0666, USA  
J. Biol. Chem. (2001), 276(21), 17920-17931

SOURCE: CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular

Biology  
Journal

DOCUMENT TYPE: English

LANGUAGE: English

AB Dendritic cells (DCs) are antigen-presenting cells that play a major role  
in initiating primary immune responses. The authors have utilized two  
independent approaches, DNA microarrays and proteomics, to analyze the  
expression profile of human CD14+ blood monocytes and their derived DCs.  
Anal. of gene expression changes at the RNA level using oligonucleotide  
microarrays complementary to 6300 human genes showed that apprx.40% of  
the genes were expressed in DCs. A total of 255 genes (4%) were regulated  
during DC differentiation or maturation. Most of these genes were not

previously assocd. with DCs and included genes encoding secreted proteins as well as genes involved in cell adhesion, signaling, and lipid metab. Protein anal. of the same cell populations was done using two-dimensional gel electrophoresis. A total of 900 distinct protein spots were included, and 4% of them exhibited quant. changes during DC differentiation and maturation. Differentially expressed proteins were identified by mass spectrometry and found to represent proteins with Ca<sup>2+</sup> binding, fatty acid binding, or chaperone activities as well as proteins involved in cell motility. In addn., proteomic anal. provided an assessment of post-translational modifications. The chaperone protein, calreticulin, was found to undergo cleavage, yielding a novel form. The combined oligonucleotide microarray and proteomic approaches have uncovered novel genes assocd. with DC differentiation and maturation and has allowed anal. of post-translational modifications of specific proteins as part of these processes.

CC 15-10 (Immunochemistry)  
Section cross-reference(s): 3, 13

IT **Mannose receptors**

RL: PRP (Properties)  
(up-regulation of gene expression in differentiation and maturation of human dendritic cells)

IT 9000-83-3, ATPase 9001-05-2, Catalase 9004-02-8, Lipoprotein lipase 9014-51-1, Indoleamine-2,3-dioxygenase 9023-99-8, Cystathione-beta-synthase 9026-00-0, Lysosomal acid lipase 9026-09-9, Phenol sulfotransferase 9027-35-4, L-Arginine:glycine amidinotransferase 9029-97-4, 3-Oxoacyl-CoA thiolase 9030-42-6 9030-96-0, IsoleucyltRNA synthetase 9035-39-6, Cytochrome b5 9075-81-4, Sialyltransferase ST6GalI 80146-85-6, Transglutaminase 82249-77-2, 15-Lipoxygenase 87683-70-3, Pterin-4a-carbinolamine dehydratase 169592-54-5, Protease inhibitor 6

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(up-regulation of gene expression in differentiation and maturation of human dendritic cells)

REFERENCE COUNT: 53

REFERENCE(S):

- (1) Arnold-Schild, D; J Immunol 1999, V162, P3757 HCAPLUS
- (2) Ashkar, S; Science 2000, V287, P860 HCAPLUS
- (4) Baggioolini, M; Int J Immunopharmacol 1995, V17, P103 HCAPLUS
- (5) Bagnard, D; Development 1998, V125, P5043 HCAPLUS
- (6) Banchereau, J; Annu Rev Immunol 2000, V18, P767 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:338762 HCAPLUS

DOCUMENT NUMBER: 134:362292

TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile

INVENTOR(S): Farr, Spencer

PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA

SOURCE: PCT Int. Appl., 222 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,

HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398 P 19991105  
 US 2000-196571 P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to det. the hypersensitivity of individuals to a given agent, such as drug or other chem., in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes assocd. with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes assocd. with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes assocd. with hypersensitivity. The expression of the genes predetd. to be assocd. with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and app. useful for identifying hypersensitivity in a subject are also disclosed.

IC ICM C12Q001-68  
 ICS G01N033-50

CC 3-4 (Biochemical Genetics)

Section cross-reference(s): 1, 6, 7, 13, 15

IT Gene, animal  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (mannose receptor; methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT Mannose receptors  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

IT 107-97-1, Sarcosin 447-41-6, Nylidrin 8056-51-7 9000-86-6, Alanine aminotransferase 9000-97-9 9001-05-2, Catalase 9001-40-5, Glucose-6-phosphate dehydrogenase 9001-48-3, Glutathione reductase 9001-50-7, Glyceraldehyde 3-phosphate dehydrogenase 9001-62-1, Hepatic lipase 9001-84-7, Phospholipase A2 9002-03-3, Dihydrofolate reductase 9002-06-6, Thymidine kinase 9002-12-4, Urate oxidase 9002-67-9, Luteinizing hormone 9003-99-0, Myeloperoxidase 9012-25-3, Catechol-O-methyltransferase 9012-38-8, PAPS synthetase 9012-39-9, 9012-52-6, S-Adenosylmethionine synthetase 9013-08-5, Phosphoenolpyruvate carboxykinase 9013-18-7, Fatty acyl-CoA synthetase 9013-38-1, Dopamine .beta.-hydroxylase 9013-66-5, Glutathione peroxidase 9013-79-0, Neuropathy target esterase 9014-55-5, Tyrosine aminotransferase 9015-71-8, Corticotropin releasing hormone 9015-81-0, 17-.beta. Hydroxysteroid dehydrogenase 9016-12-0, Hypoxanthine-guanine phosphoribosyltransferase 9023-44-3, Tryptophanyl-tRNA synthetase 9023-62-5, Glutathione synthetase 9023-64-7, .gamma.-Glutamylcysteinyl synthetase 9023-70-5, Glutamine synthetase 9024-60-6, Ornithine decarboxylase 9024-61-7, Histidine decarboxylase 9025-32-5, Prolidase 9026-00-0, Cholesterol esterase 9026-09-9, Phenol sulfotransferase 9026-43-1, Serine kinase 9026-51-1, Nucleoside diphosphate kinase 9027-13-8, Enoyl-CoA hydratase 9027-65-0, Acyl-CoA dehydrogenase 9028-06-2 9028-31-3, Aldose reductase 9028-35-7, HMG

CoA reductase 9028-41-5, Hydroxyacyl-Coenzyme A dehydrogenase  
 9028-86-8, Aldehyde dehydrogenase 9029-73-6, Phenyl alanine hydroxylase  
 9029-80-5, Histamine N-methyltransferase 9029-97-4, 3-Ketoacyl-CoA  
 thiolase 9031-37-2, Ceruloplasmin 9031-54-3, Sphingomyelinase  
 9031-61-2, Thymidylate synthase 9031-72-5, Alcohol dehydrogenase  
 9032-20-6, DT-Diaphorase 9035-58-9, Blood-coagulation factor III  
 9036-22-0, Tyrosine hydroxylase 9037-21-2, Tryptophan hydroxylase  
 9037-62-1, Glycyl tRNA synthetase 9039-06-9, NADPH cytochrome P450  
 reductase 9040-57-7, Ribonucleotide reductase 9041-92-3 9045-77-6,  
 Fatty acid synthase 9046-27-9, .gamma.-Glutamyl transpeptidase  
 9048-63-9, Epoxide hydrolase 9055-67-8, Poly(ADP-ribose)polymerase  
 9059-25-0, Lysyl oxidase 9068-41-1, Carnitine palmitoyltransferase  
 9074-02-6, Malic enzyme 9074-10-6, Biliverdin reductase 9074-19-5,  
 Hydratase 9074-87-7, .gamma.-Glutamyl hydrolase 9081-36-1,  
 25-Hydroxyvitamin D3 1-hydroxylase 11096-26-7, Erythropoietin  
 37205-63-3, ATP synthase 37237-44-8, Glucosylceramide synthase  
 37289-06-8, Acid ceramidase 37318-49-3, Protein disulfide isomerase  
 39391-18-9, Prostaglandin H synthase 52228-01-0 56093-23-3,  
 .alpha.-1,2-Fucosyl transferase 56645-49-9, Cathepsin G 59536-73-1,  
 Phosphomannomutase 59536-74-2, Very long-chain acyl-CoA dehydrogenase  
 60267-61-0, Ubiquitin 60616-82-2, Cathepsin L 61116-22-1, Fatty  
 acyl-CoA oxidase 62229-50-9, Epidermal growth factor 67339-09-7,  
 Thiopurine methyltransferase 67763-96-6, Insulin-like growth factor 1  
 67763-97-7, Insulin-like growth factor II 77271-19-3,  
 6-O-Methylguanine-DNA methyltransferase 77847-96-2, Prostacyclin-  
 stimulating factor 79747-53-8, Protein tyrosine phosphatase  
 79955-99-0, Stromelysin-1 80146-85-6, Tissue Transglutaminase  
 80295-41-6, Complement component C3 81627-83-0, Colony stimulating  
 factor -1 82391-43-3, 12-Lipoxygenase 83268-44-4 83869-56-1,  
 Granulocyte-macrophage colony-stimulating factor 85637-73-6, Atrial  
 natriuretic factor 87397-91-9, Thymosin .beta.10 88943-21-9,  
 Proteinase .alpha.1-inhibitor III 89964-14-7, Prothymosin, alpha  
 90698-26-3, Ribosomal protein S6 kinase 92767-51-6, O-6-Alkylguanine-DNA-  
 alkyltransferase 96024-44-1, Granulin 105238-46-8, Macropain  
 106096-92-8, Fibroblast growth factor, acidic 106956-32-5, Oncostatin M  
 112130-98-0, Procathepsin L 114949-22-3, Activin (protein)  
 117698-12-1, Paraoxonase 119418-04-1, Galanin 123626-67-5,  
 Endothelin-1 125978-95-2, Nitric oxide synthase 127464-60-2, Vascular  
 endothelial growth factor 137632-07-6, Extracellular-signal-regulated  
 kinase 1 138238-81-0, Endothelin converting enzyme-1 140208-24-8,  
 Tissue inhibitor of metalloproteinase-1 141176-92-3 141349-86-2,  
 Cyclin dependent kinase 2 141436-78-4, Protein kinase C 142243-03-6,  
 Plasminogen activator inhibitor 2 142805-56-9, DNA topoisomerase II  
 142805-58-1, MAP kinase kinase 143180-75-0, DNA topoisomerase I  
 143375-65-9, Cyclin dependent kinase 1 145809-21-8, Tissue inhibitor of  
 metalloproteinase-3 146480-35-5, Matrix metalloproteinase-2  
 147014-97-9, Cyclin dependent kinase 4 148348-15-6, Fibroblast growth  
 factor 7 149316-81-4, Branched chain acyl-CoA oxidase 149371-05-1,  
 Kinase (phosphorylating), gene c-abl protein 149885-78-9, Hepatocyte  
 growth factor activator 154907-65-0, Checkpoint kinase 155807-64-0,  
 FEN-1 Endonuclease 165245-96-5, p38 Mitogen-activated protein kinase  
 169592-56-7, CPP32 proteinase 179241-70-4, Protein kinase ZPK  
 179241-78-2, Caspase 8 182372-14-1, Caspase 2 182372-15-2, Caspase 6  
 182762-08-9, Caspase 4 187414-12-6, Caspase-1 189258-14-8, Caspase 7  
 192465-11-5, Caspase 5 193363-12-1, Vascular endothelial growth factor D  
 194554-71-7, Tissue factor pathway inhibitor 205944-50-9,  
 Osteoprotegerin 220983-94-8, Sorbitol dehydrogenase 289898-51-7, JNK1  
 protein kinase 303752-61-6, DNA dependent protein kinase 329736-03-0,  
 Cytochrome p450 3A4 329764-85-4, Cytochrome p450 1A1 329900-75-6,  
 Cyclooxygenase 2 329978-01-0, Cytochrome p450 2C9 330196-64-0,  
 Cytochrome p450 1A2 330196-93-5, Cytochrome p450 2E1 330197-98-3,  
 Cytochrome p 450 1A1 330207-10-8, Cytochrome p450 2B1 330589-90-7,  
 Cytochrome p450 2C19 330596-22-0, Cytochrome p450 1B1 330597-62-1,

Cytochrome p450 2D6 330975-22-9, Macrostatin 331462-97-6, Cytochrome p450 2B2 331462-98-7, Cytochrome p450 3A1 331823-00-8, Cytochrome p450 2C11 331823-12-2, Cytochrome p450 2C12 331823-27-9, Cytochrome p450 2A1 331827-06-6, Cytochrome p450 2A6 332847-52-6, Cytochrome p450 4A 336884-26-5, Cytochrome p450 2B10 338964-08-2, P 450 17A 338969-62-3, P 450 2A3 338969-69-0, P 450 2F2 338969-71-4, P 450 4A1  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (methods of detg. individual hypersensitivity to a pharmaceutical agent from gene expression profile)

L34 ANSWER 4 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1999:582072 HCPLUS  
 DOCUMENT NUMBER: 132:120869  
 TITLE: Splice-site mutations in atherosclerosis candidate genes: relating individual information to phenotype  
 Von Kodolitsch, Yskert; Pyeritz, Reed E.; Rogan, Peter K.  
 AUTHOR(S): Department of Cardiology, University Hospital Eppendorf, Hamburg, Germany  
 CORPORATE SOURCE: Circulation (1999), 100(7), 693-699  
 SOURCE: CODEN: CIRCAZ; ISSN: 0009-7322  
 PUBLISHER: Lippincott Williams & Wilkins  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Nucleotide variants in several genes for lipid and methionine metab. influence the risk of premature atherosclerosis. Ten percent of single nucleotide substitutions in these genes involve mRNA splice sites. The effects of some of these changes on splicing and on phenotypic severity are not inherently obvious. Using an information theory-based model, the individual information content ( $R_i$ , in bits) of splice sites adjacent to 289 mutations (including 31 splice-site mutations) in the atherosclerosis candidate genes APOAI, APOB, APOCII, APOE, CBS, CETP, LCAT, LIPA, LDLR, and LPL was measured. The predictions of information anal. were then corroborated by published mRNA analyses. The  $R_i$  values of mutant sites were consistent with either complete or partial inactivation of these sites. Seven mutations were predicted to activate cryptic splice sites. Predicted inactive mutant sites were assocd. with either "av." or "severe" dyslipidemia and commensurate redns. in protein levels or activity, whereas mutations expected to exhibit residual splicing had av. or "mild" effects on lipid and protein expression. Information anal. of splice-junction variants in atherosclerosis candidate genes distinguishes inactive from leaky splice sites and identifies activated cryptic sites. Predicted changes in splicing were related to phenotypic severity.  
 CC 14-5 (Mammalian Pathological Biochemistry)  
 ST Section cross-reference(s): 3  
 gene atherosclerosis splice site mutation phenotype  
 IT Apolipoproteins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (A-II, gene; splice-site mutations in atherosclerosis candidate genes in humans in relation to phenotype)  
 IT Gene, animal  
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)  
 (APOAI; splice-site mutations in atherosclerosis candidate genes in humans in relation to phenotype)  
 IT Gene, animal  
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)  
 (APOB; splice-site mutations in atherosclerosis candidate genes in humans in relation to phenotype)  
 IT Gene, animal  
 RL: ADV (Adverse effect, including toxicity); BPR (Biological process);

PRP (Properties); BIOL (Biological study); PROC (Process)  
(APOCII; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);  
PRP (Properties); BIOL (Biological study); PROC (Process)  
(APOE; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Apolipoproteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(B, gene; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Apolipoproteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(C-II, gene; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);  
PRP (Properties); BIOL (Biological study); PROC (Process)  
(CBS; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);  
PRP (Properties); BIOL (Biological study); PROC (Process)  
(CETP; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Apolipoproteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(E, gene; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);  
PRP (Properties); BIOL (Biological study); PROC (Process)  
(LCAT; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Lipoprotein receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(LDL, gene; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);  
PRP (Properties); BIOL (Biological study); PROC (Process)  
(LDLR; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);  
PRP (Properties); BIOL (Biological study); PROC (Process)  
(LIPA; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Gene, animal  
RL: ADV (Adverse effect, including toxicity); BPR (Biological process);  
PRP (Properties); BIOL (Biological study); PROC (Process)  
(LPL; splice-site mutations in atherosclerosis  
candidate genes in humans in relation to phenotype)

IT Proteins, specific or class  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(cholesterol ester-exchanging, gene; splice-site mutations in  
atherosclerosis candidate genes in humans in relation to  
phenotype)

IT Lipoproteins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(low-d., gene; splice-site mutations in  
atherosclerosis candidate genes in humans in relation to

phenotype)  
 IT RNA splicing  
 (messenger; splice-site mutations in atherosclerosis  
 candidate genes in humans in relation to phenotype)  
 IT Mutation  
 (splice site; splice-site mutations in  
 atherosclerosis candidate genes in humans in relation to  
 phenotype)  
 IT Atherosclerosis  
 Mutation  
 Phenotypes  
 Risk assessment  
 Transcription, genetic  
 (splice-site mutations in atherosclerosis candidate  
 genes in humans in relation to phenotype)  
 IT mRNA  
 RL: PRP (Properties)  
 (splice-site mutations in atherosclerosis candidate  
 genes in humans in relation to phenotype)  
 IT Pre-mRNA  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 RL: BPR (Biological process); BIOL (Biological study)  
 (splicing; splice-site mutations in atherosclerosis  
 candidate genes in humans in relation to phenotype)  
 IT 9023-99-8, Cystathione .beta.-synthase 9026-00-0,  
 Lysosomal acid lipase 9031-14-5, Lecithin  
 cholesterol acyltransferase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (gene; splice-site mutations in atherosclerosis  
 candidate genes in humans in relation to phenotype)

REFERENCE COUNT: 45  
 REFERENCE(S):  
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 (2) Bruun, T; J Lipid Res 1993, V34, P2109 HCAPLUS  
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 V187, P620 HCAPLUS  
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 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1999:246744 HCAPLUS  
 DOCUMENT NUMBER: 131:86054  
 TITLE: Cholesteryl ester hydrolase deficiency  
 AUTHOR(S): Maslen, C. L.; Illingworth, D. R.  
 CORPORATE SOURCE: Division of Endocrinology, Diabetes & Clinical  
 Nutrition, Oregon Health Sciences University,  
 Portland, OR, USA  
 SOURCE: Lipoproteins Health Dis. (1999), 847-861. Editor(s):  
 Betteridge, D. J.; Illingworth, D. Roger; Shepherd,  
 James. Arnold: London, UK.  
 CODEN: 670GA9  
 DOCUMENT TYPE: Conference; General Review  
 LANGUAGE: English  
 AB A review, with 94 refs. Topics discussed include: clin. features, tissue  
 and plasma lipid profiles, genetics, and diagnosis of cholesteryl ester  
 hydrolase deficiency, genetic variation of cholesteryl ester hydrolase  
 activity and premature atherosclerosis, clin. intervention, and animal  
 model.  
 CC 14-0 (Mammalian Pathological Biochemistry)  
 ST review Wolman disease clin feature genetics diagnosis  
 intervention; cholesterol ester hydrolase deficiency review  
 IT Disease models  
 (Wolman's disease; clin. features, diagnosis, and genetics of  
 and interventions for human cholesteryl ester hydrolase deficiency)

IT Disease, animal  
 (Wolman's; clin. features, diagnosis, and genetics of and interventions for human cholestryl ester hydrolase deficiency)

IT Atherosclerosis  
 Diagnosis  
 Genetics  
 (clin. features, diagnosis, and genetics of and interventions for human cholestryl ester hydrolase deficiency)

IT 9026-00-0, Cholestryl ester hydrolase  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (clin. features, diagnosis, and genetics of and interventions for human cholestryl ester hydrolase deficiency)

REFERENCE COUNT: 20  
 REFERENCE(S):  
 (1) Rothschild, C; Genomics 1992, V13, P25 HCPLUS  
 (2) Sando, G; Journal of Biological Chemistry 1985,  
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 Vascular Biology 1995, V15, P773 HCPLUS  
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 V270, P27766 HCPLUS  
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 V256, P2952 HCPLUS  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 6 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1998:412362 HCPLUS  
 DOCUMENT NUMBER: 129:197833  
 TITLE: Hormone-sensitive lipase overexpression increases  
 cholestryl ester hydrolysis in macrophage foam cells  
 Escary, Jean-Louis; Choy, Henry A.; Reue, Karen;  
 Schotz, Michael C.  
 AUTHOR(S):  
 CORPORATE SOURCE: Lipid Research Laboratory, West Los Angeles VA Medical  
 Center, University of California, Los Angeles, CA,  
 90073, USA  
 SOURCE: Arterioscler., Thromb., Vasc. Biol. (1998), 18(6),  
 991-998  
 CODEN: ATVBFA; ISSN: 1079-5642

PUBLISHER: Williams & Wilkins  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Atherosclerosis is a complex physiopathol. process initiated by the formation of cholesterol-rich lesions in the arterial wall. Macrophages play a crucial role in this process because they accumulate large amts. of cholesterol esters (CEs) to form the foam cells that initiate the formation of the lesion and participate actively in the development of the lesion. Therefore, prevention or reversal of CE accumulation in macrophage foam cells could result in protection from multiple pathol. effects. In this report, we show that the CE hydrolysis catalyzed by neutral cholesterol ester hydrolase (nCEH) can be modulated by overexpression of hormone-sensitive lipase (HSL) in macrophage foam cells. For these studies, RAW 264.7 cells, a murine macrophage cell line, were found to be a suitable model of foam cell formation. HSL expression and nCEH activity in these cells and in peritoneal macrophages were comparable. In addn., antibody titrn. showed that essentially all nCEH activity in murine macrophages was accounted for by HSL. To examine the effect of HSL overexpression on foam cell formation, RAW 264.7 cells were stably transfected with a rat HSL cDNA. The resulting HSL overexpression increased hydrolysis of cellular CEs 2- to 3-fold in lipid-laden cells in the presence of an acyl CoA:cholesterol acyltransferase (ACAT) inhibitor. Furthermore, addn. of cAMP produced a 5-fold higher rate of CE hydrolysis in cholesterol-laden, HSL-overexpressing cells than in control cells and resulted in nearly complete hydrolysis of cellular CEs in only 9 h, compared with <50% hydrolysis in control cells. Thus, HSL overexpression

stimulated the net hydrolysis of CEs, leading to faster hydrolysis of lipid deposits in model foam cells. These data suggest that HSL overexpression in macrophages, alone or in combination with ACAT inhibitors, may constitute a useful therapeutic approach for impeding CE accumulation in macrophages *in vivo*.

CC 1-10 (Pharmacology)  
 ST Section cross-reference(s): 3  
 atherosclerosis gene therapy cholesterol  
 metab macrophage; cholestryl esterase lipase expression gene  
 therapy  
 IT Antiatherosclerotics  
 Anticholesteremic agents  
 Atherosclerosis  
 Gene expression  
 Gene therapy  
 Macrophage  
 (hormone-sensitive lipase overexpression increases cholestryl ester  
 hydrolysis in macrophage foam cells in relation to  
 atherosclerosis therapy)  
 IT Blood cholesterol  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (hormone-sensitive lipase overexpression increases cholestryl ester  
 hydrolysis in macrophage foam cells in relation to  
 atherosclerosis therapy)  
 IT 9001-62-1, Lipase  
 RL: BAC (Biological activity or effector, except adverse); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (hormone-sensitive lipase overexpression increases cholestryl ester  
 hydrolysis in macrophage foam cells in relation to  
 atherosclerosis therapy)  
 IT 57-88-5D, Cholesterol, esters 9026-00-0, Neutral cholestryl  
 ester hydrolase  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (hormone-sensitive lipase overexpression increases cholestryl ester  
 hydrolysis in macrophage foam cells in relation to  
 atherosclerosis therapy)  
 IT 9027-63-8, Cholesterol acyltransferase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors; hormone-sensitive lipase overexpression increases  
 cholestryl ester hydrolysis in macrophage foam cells in relation to  
 atherosclerosis therapy)

L34 ANSWER 7 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 1998:223121 HCPLUS

ACCESSION NUMBER:

128:307050

DOCUMENT NUMBER:

Immunohistochemical demonstration of enzymically modified human LDL and its colocalization with the terminal complement complex in the early atherosclerotic lesion

TITLE:

Torzewski, Michael; Klouche, Mariam; Hock, Johann;  
 Messner, Martina; Dorweiler, Bernhard; Torzewski, Jan;  
 Gabbert, Helmut Erich; Bhakdi, Sucharit  
 Institute of Pathology, University of Dusseldorf,  
 Dusseldorf, Germany

AUTHOR(S):

*Vasc. Biol.* (1998), 18(3),  
*Arterioscler., Thromb.,*

CORPORATE SOURCE:

369-378

SOURCE:

CODEN: ATVBFA; ISSN: 1079-5642

Williams & Wilkins

PUBLISHER:

Journal

DOCUMENT TYPE:

English

LANGUAGE:

AB Treatment of low d. lipoprotein (LDL) with degrading enzymes transforms the mol. to a moiety that is micromorphol. indistinguishable from lipoproteinaceous particles that are present in atherosclerotic plaques,

and enzymically modified LDL (E-LDL), but not oxidized LDL (ox-LDL), spontaneously activates the alternative complement pathway, as do lesion lipoprotein derivs. Furthermore, because E-LDL is a potent inducer of macrophage foam cell formation, the authors propose that enzymic degrdn. may be the key process that renders LDL atherogenic. In this article, the authors report the prodn. of two murine monoclonal antibodies recognizing cryptic epitopes in human apolipoprotein B that become exposed after enzymic attack on LDL. One antibody reacted with LDL after single treatment with trypsin, whereas recognition by the second antibody required combined treatment of LDL with trypsin and cholesterol esterase. In ELISAs, both antibodies reacted with E-LDL produced in vitro and with lesion complement activator derived from human atherosclerotic plaques, but they were unreactive with native LDL or ox-LDL. The antibodies stained E-LDL, but not native LDL or ox-LDL, that had been artificially injected into arterial vessel walls. With the use of these antibodies, the authors have demonstrated that early human atherosclerotic coronary lesions obtained at autopsy as well as lesions exmd. in freshly explanted hearts always contain extensive extracellular deposits of E-LDL. Terminal complement complexes, detected with a monoclonal antibody specific for a C5b-9 neoepitope, colocalized with E-LDL within the intima, which is compatible with the proposal that subendothelialy deposited LDL is enzymically transformed to a complement activator at the earliest stages in lesion development.

CC 14-5 (Mammalian Pathological Biochemistry)  
Section cross-reference(s): 15

IT Coronary artery disease  
(atherosclerosis; immunohistochem. demonstration of enzymically modified human LDL and colocalization with terminal complement complex in early atherosclerotic lesion)

IT Atherosclerosis  
(coronary; immunohistochem. demonstration of enzymically modified human LDL and colocalization with terminal complement complex in early atherosclerotic lesion)

IT Atherosclerosis  
(plaque; immunohistochem. demonstration of enzymically modified human LDL and colocalization with terminal complement complex in early atherosclerotic lesion)

IT 9002-07-7, Trypsin 9026-00-0, Cholesterol esterase  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BIOL (Biological study)  
(LDL treated with; immunohistochem. demonstration of enzymically modified human LDL and colocalization with terminal complement complex in early atherosclerotic lesion)

L34 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 1997:280151 HCAPLUS  
DOCUMENT NUMBER: 126:315913  
TITLE: Altered mononuclear phagocyte differentiation  
associated with genetic defects of the  
lysosomal acid lipase  
AUTHOR(S): Rothe, Gregor; Stohr, Josef; Fehringer, Petra; Gasche,  
Christoph; Schmitz, Gerd  
CORPORATE SOURCE: Institute for Clinical Chemistry and Laboratory  
Medicine, University of Regensburg, Regensburg,  
D-93042, Germany  
SOURCE: Atherosclerosis (Shannon, Irel.) (1997), 130(1,2),  
215-221  
CODEN: ATHSBL; ISSN: 0021-9150  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Multiparameter flow cytometry reveals a complex heterogeneity of

mononuclear phagocyte differentiation within the peripheral blood compartment. In this study, the relation of abnormal cellular lipid metab. to the phenotype of peripheral blood mononuclear phagocytes, which finally may be related to atherogenesis, was analyzed using recently characterized autosomal recessive defects of lysosomal acid lipase (LAL) expression as model system. The redn. of LAL activity in nine heterozygote, disease free carriers of mutations from two cholestryl ester storage disease (CESD) pedigrees and the family of a patient with Wolman disease was assocd. with an increased fraction of monocytes which expressed CD56 (N-CAM) (4.1% of monocytes, compared to 2.2% in ten controls), an antigen characteristic of immature myeloid cells, suggesting an increased turnover of monocytes. Furthermore, a trend was obsd. towards an enhanced blood pool of more mature mononuclear phagocytes which show decreased expression of the 55 kDa lipopolysaccharide receptor (CD14) together with either expression of the Fc-.gamma.-receptor III (CD16) or a high expression of CD33. A similar phenotype of peripheral mononuclear phagocytes was obsd. in the two CESD patients analyzed. In conclusion, the authors' data suggest that these monogenetic defects of lysosomal lipoprotein metab. are assocd. with complex alterations of mononuclear phagocyte differentiation and extravasation.

CC 14-14 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 3

ST mononuclear phagocyte differentiation **lysosomal acid lipase**

IT CD antigens

RL: BOC (Biological occurrence); BIOL (Biological study); OCCU  
(Occurrence)  
(CD33; altered mononuclear phagocyte differentiation assocd. with genetic defects of human **lysosomal acid lipase** in relation to myeloid proteins, **cholestryl ester storage** disease, **Wolman** disease, and atherogenesis)

IT Lipid metabolic diseases

(**Wolman's** disease; altered mononuclear phagocyte differentiation assocd. with genetic defects of human **lysosomal acid lipase** in relation to myeloid proteins, **cholestryl ester storage** disease, **Wolman** disease, and atherogenesis)

IT **Atherosclerosis**

Heterozygosity

Monocyte

Monocytopoiesis

Mononuclear phagocyte

**Mutation**

Myeloid precursor cell  
(altered mononuclear phagocyte differentiation assocd. with genetic defects of human **lysosomal acid lipase** in relation to myeloid proteins, **cholestryl ester storage** disease, **Wolman** disease, and atherogenesis)

IT Fc.gamma.RIII receptors

Lipopolysaccharide-binding protein

N-CAM (cell adhesion molecule)

RL: BOC (Biological occurrence); BIOL (Biological study); OCCU

(Occurrence)  
(altered mononuclear phagocyte differentiation assocd. with genetic defects of human **lysosomal acid lipase** in relation to myeloid proteins, **cholestryl ester storage** disease, **Wolman** disease, and atherogenesis)

IT Lipid metabolic diseases

(**cholesterol ester storage** disease; altered mononuclear phagocyte differentiation assocd. with genetic defects of human **lysosomal acid lipase** in relation to myeloid proteins and)

IT 9026-00-0, Cholesterol esterase  
 RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);  
 PRP (Properties); BIOL (Biological study); OCCU (Occurrence)  
 (altered mononuclear phagocyte differentiation assocd. with genetic  
 defects of human lysosomal acid lipase in  
 relation to myeloid proteins, cholestry1 ester  
 storage disease, Wolman disease, and atherogenesis)

L34 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:383196 HCAPLUS  
 DOCUMENT NUMBER: 125:56240  
 TITLE: Complementarily bonded two- and three-dimensional supramolecular structures  
 INVENTOR(S): Virtanen, Jorma; Virtanen, Sinikka  
 PATENT ASSIGNEE(S): Burstein Laboratories, Inc., USA  
 SOURCE: PCT Int. Appl., 70 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9613522	A1	19960509	WO 1995-US13990	19951030
W: AL, AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2203875	AA	19960509	CA 1995-2203875	19951030
AU 9641973	A1	19960523	AU 1996-41973	19951030
EP 789715	A1	19970820	EP 1995-940569	19951030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10508304	T2	19980818	JP 1995-514797	19951030
PRIORITY APPLN. INFO.:			US 1994-332514	19941031
			WO 1995-US13990	19951030

AB The present invention relates to supramols. which are formed by at least two components. Each component comprises an effector mol. and at least one nucleic acid chain. The nucleic acid chains of each component are complementary to nucleic acid chains on other components and thus are able to bind the components of the supramol. by the formation of double stranded nucleic acid chains between the complementary chains. The present invention also relates to a method of making the supramols. of the present invention. The nucleic acid chains are preferably DNA, RNA, and present invention. The nucleic acid chains are structural analogs of DNA or RNA. Effector mols. that may also be used to form the supramols. include, but are not limited to polypeptides, lipids, sugars. These effector mols. may impart chem., phys. properties to the supramol. that include, but are not limited to hydrophobicity, hydrophilicity, electron cond., fluorescence, radioactivity, biol. activity, cellular toxicity, catalytic activity, mol. and cellular recognition and in vivo transport selectivity. The supramol. is useful for electronics, immunoassay, and diagnosis and treatment of disease, e.g. cancer, atherosclerosis, virus infection. Demonstrated in example was prepn. of supramol. contg. monoclonal anti-gp41/160 antibody, oligonucleotide and enzyme such as phospholipase A2, lipase, RNase and carboxypeptidase for capturing virus particles.

IC ICM C07K016-00  
 ICS C07K017-00; C07K017-14  
 CC 15-3 (Immunochemistry)  
 Section cross-reference(s): 3  
 IT Neoplasm

(marker protein; supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT Virus  
(protein; supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT Molecules  
(supra-; supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT Antibodies

Enzymes

Ligands

Nucleic acids

Receptors

RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(supramol.; supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT Proteins, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(virus; supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT Antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(CD4, supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT Arteriosclerosis

(atherosclerosis, supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT Glycoproteins, specific or class

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(gp160, supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT Glycoproteins, specific or class

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(gp41, supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT Antibodies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monoclonal, to gp41/160; supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT Virus, animal

(retro-, supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT 9001-84-7P, Phospholipase A2 9001-99-4P, RNase 9031-98-5P,

Carboxypeptidase

RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified); MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(supramol. contg. antibody and oligonucleotide and enzyme for electronics, immunoassay, and **disease diagnosis and treatment**)

IT 9001-62-1P, Lipase 9013-93-8P, Phospholipase 9026-00-OP,  
**Cholesterol esterase** 9026-81-7P, Nuclease  
 RL: BPN (Biosynthetic preparation); BUU (Biological use, unclassified);  
 MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (supramol.; supramol. contg. antibody and oligonucleotide and enzyme  
 for electronics, immunoassay, and disease diagnosis and  
 treatment)

L34 ANSWER 10 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1991:628985 HCPLUS  
 DOCUMENT NUMBER: 115:228985  
 TITLE: Acid hydrolases in early and late endosome fractions  
 from rat liver  
 AUTHOR(S): Runquist, Elizabeth A.; Havel, Richard J.  
 CORPORATE SOURCE: Cardiovasc. Res. Inst., Univ. California, San  
 Francisco, CA, 94143-0130, USA  
 SOURCE: J. Biol. Chem. (1991), 266(33), 22557-63  
 CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The distribution of the cation-independent mannose 6-phosphate receptor  
 and 5 acid hydrolases was examd. in early and late endosomes and a  
 receptor-recycling fraction isolated from livers of estradiol-treated  
 rats. Enrichment of mannose 6-phosphate receptor mass relative to that of  
 crude liver membranes was comparable in membranes of early and late  
 endosomes but was even greater in membranes of the receptor-recycling  
 fraction. Enrichment of acid hydrolase activities (aryl sulfatase,  
 N-acetyl-.beta.-glucosaminidase, tartrate-sensitive acid phosphatase, and  
 cholesteryl ester acid hydrolase) and cathepsin D mass was also comparable  
 in early and late endosomes but was considerably lower in the  
 receptor-recycling fraction. The enrichment of 2 acid hydrolases, acid  
 phosphatase and cholesteryl ester acid hydrolase, in endosomes was  
 severalfold greater than that of the other 3 examd., .apprx.40% of that  
 found in lysosomes. Acid phosphatase and cholesteryl ester acid hydrolase  
 were partially assocd. with endosome membranes, whereas cathepsin D was  
 found entirely in the endosome contents. These findings raise the  
 possibility that lysosomal enzymes traverse early endosomes during  
 transport to lysosomes in rat hepatocytes and suggest that the greater  
 enrichment of some acid hydrolases in endosomes is related to their  
 assocn. with endosome membranes. Despite the substantial enrichment of  
 lysosomal enzymes in hepatocytic endosomes, it was found that 2,  
 cholesteryl ester acid hydrolase and cathepsin D, did not degrade  
 cholesteryl esters and apolipoprotein B-100 of endocytosed low-d.  
 lipoproteins in vivo, presumably because they are inactive at the pH  
 within endosomes.

CC 13-1 (Mammalian Biochemistry)

IT Receptors

RL: BIOL (Biological study)  
 (for **mannose** phosphate, of early and late endosomes of liver)  
 9012-33-3, .beta.-N-Acetylglucosaminidase 9016-17-5, Aryl sulfatase

IT 9025-26-7, Cathepsin D 9026-00-0

RL: BIOL (Biological study)  
 (of early and late endosomes, of liver)

IT 3672-15-9, **Mannose** 6-phosphate

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (receptors, of early and late endosomes of liver)

L34 ANSWER 11 OF 14 HCPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:444672 HCPLUS  
 DOCUMENT NUMBER: 115:444672  
 TITLE: Cholesterol esterases  
 AUTHOR(S): Fujiyama, Jiro; Kuriyama, Masaru

CORPORATE SOURCE: Med. Sch., Kagoshima Univ., Kagoshima, Japan  
 SOURCE: Lipid (1991), 2(1), 33-42  
 CODEN: LIPDET  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: Japanese  
 AB A review with 35 refs., on cholesterol esterases (CE), including acid, neutral, and pancreatic CE, discussing their reaction kinetics, regulation, detn., and function (esp. in cholesterol metab.) and clin. significance in diseases such as cholesterol ester storage disease, atherosclerosis, etc.  
 CC 7-0 (Enzymes)  
 Section cross-reference(s): 14  
 ST review cholesterol esterase; disease  
 cholesterol esterase review  
 IT Atherosclerosis  
 (cholesterol esterase in)  
 IT Xanthomatosis  
 (Wolman's disease, cholesterol esterase  
 in)  
 IT Lipids, biological studies  
 RL: BIOL (Biological study)  
 (metabolic disorders, cholesterol ester storage  
 disease, cholesterol esterase in)  
 IT 9026-00-0, Cholesterol esterase  
 RL: BIOL (Biological study)  
 (properties and function and clin. significance of)

L34 ANSWER 12 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1991:21353 HCPLUS  
 DOCUMENT NUMBER: 114:21353  
 TITLE: Intercellular transport of lysosomal  
 acid lipase mediates lipoprotein  
 cholestryl ester metabolism in a human vascular  
 endothelial cell-fibroblast coculture system  
 Sando, Gloria N.; Ma, Guo Ping; Lindsley, Kathy A.;  
 Wei, Yu Ping  
 AUTHOR(S):  
 CORPORATE SOURCE: Cent. Res., Univ. Iowa, Iowa City, IA, 52242, USA  
 SOURCE: Cell Regul. (1990), 1(9), 661-74  
 CODEN: CELREQ; ISSN: 1044-2030  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Results are presented from studies of human cell culture models to support the premise that the extracellular transport of lysosomal acid lipase has a function in lipoprotein cholestryl ester metab. in vascular tissue. Vascular endothelial cells secreted a higher fraction of cellular acid lipase than did smooth muscle cells and fibroblasts. Acid lipase and lysosomal .beta.-hexosaminidase were secreted at approx. the same rate from the apical and basolateral surface of an endothelial cell monolayer. Stimulation of secretion with NH4Cl did not affect the polarity. The ability of secreted endothelial lipase to interact with connective tissue cells and influence lipoprotein cholesterol metab. was studied in a coculture system in which endothelial cells on a micropore filter were suspended above a monolayer of acid lipase-deficient (Wolman disease) fibroblasts. After 5-7 days acid lipase activity in the fibroblasts reached 10%-20% of the level in normal cells; cholestryl esters that had accumulated from growth in serum were cleared. Addn. of mannose 6-phosphate to the coculture medium blocked acid lipase uptake and cholesterol clearance, indicating that lipase released from endothelial cells was packaged into fibroblast lysosomes by a phosphomannosyl receptor-mediated pathway. Supplementation of the coculture medium with serum was not required for lipase uptake and cholestryl ester hydrolysis by the fibroblasts, but was necessary for cholesterol clearance. Results from the coculture model suggest that acid lipase may be transported from

intact endothelium to cells in the lumen or the wall of a blood vessel. It is postulated that delivery of acid hydrolases and lipoproteins to a common endocytic compartment may occur and have an impact on cellular lipoprotein processing.

CC 13-2 (Mammalian Biochemistry)

IT Receptors

RL: BIOL (Biological study)  
(mannose phosphate, acid lipase intercellular transport  
mediated by, in human fibroblast)

L34 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1987:547123 HCAPLUS

DOCUMENT NUMBER: 107:147123

TITLE: Cholestyramine treatment in early life of low-density lipoprotein receptor deficient Watanabe rabbits: decreased aortic cholestryll ester accumulation and atherosclerosis in adult life

AUTHOR(S): Subbiah, M. T. R.; Yunker, R. L.; Rymaszewski, Z.; Kottke, B. A.; Bale, L. K.

CORPORATE SOURCE: Med. Cent., Univ. Cincinnati, Cincinnati, OH, USA  
SOURCE: Biochim. Biophys. Acta (1987), 920(3), 251-8

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of cholestyramine treatment in the early life of heritable hyperlipidemic rabbits (an animal model lacking low-d. lipoprotein receptor activity) on subsequent (6 mo recovery) occurrence of natural atherosclerotic lesion and arterial cholesterol metab. was investigated. These results show that early cholestyramine pre-treatment in a low-d. lipoprotein receptor-deficient animal model causes persistent changes which might influence cholestryll ester accumulation and atherogenesis in adult life, even after cholestyramine treatment is discontinued.

CC 1-10 (Pharmacology)

ST cholestyramine atherosclerosis lipoprotein receptor deficiency;  
aorta cholestryll ester cholestyramine; hypercholesterolemia  
cholestyramine

IT Receptors

RL: BIOL (Biological study)  
(for low-d. lipoproteins, deficiency of, cholestyramine effect on  
atherosclerosis and cholestryll ester accumulation in)

IT Atherosclerosis

(treatment of, with cholestyramine)

IT Lipoproteins

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(low-d., receptors, deficiency of, cholestyramine effect on aortic  
cholestryll ester accumulation and atherosclerosis in)

IT 11041-12-6, Cholestyramine

RL: BIOL (Biological study)  
(atherosclerosis and aortic cholestryll ester accumulation  
response to, in familial hypercholesterolemia)

IT 57-88-5, Cholesterol, biological studies

RL: BIOL (Biological study)  
(metabolic disorders, familial hypercholesterolemia,  
cholestyramine effect on aortic cholestryll ester accumulation and  
atherosclerosis in)

IT 9026-00-0, Cholesterol esterase

RL: BIOL (Biological study)  
(neutral, cholestyramine effect on, in familial hypercholesterolemia)

L34 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1984:452670 HCAPLUS

DOCUMENT NUMBER: 101:52670

TITLE: A study on the erythrocyte structures involved in the interaction with mannose-resistant *E. coli* adhesins  
 AUTHOR(S): Chiarini, F.; Mastromarino, P.; Seganti, L.; Orsi, N.  
 CORPORATE SOURCE: Fac. Med. Chirur., Univ. Roma "La Sapienza", Rome,  
 00100, Italy  
 SOURCE: Boll. Ist. Sieroter. Milan. (1983), 62(5), 420-5  
 CODEN: BISMAP; ISSN: 0021-2547  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The chem. groups of human group A erythrocytes responsible for binding mannose-resistant (MR) adhesins of uropathogenic *Escherichia coli* were investigated. Chymotrypsin and papain reduced hemagglutination by *E. coli*, whereas trypsin had no effect. Phospholipases (A2, C, and D) decreased the hemagglutination, but cholesterol esterase increased it 3-6-fold. Neuraminidase treatment increased the *E. coli* affinity of the erythrocytes; removal of galactose and fucose returned the affinity to control values. In addn. to the enzymic degrdn. studies, a series of competition expts. was conducted. The effects of human serum proteins, phospholipids, cholesterol, and carbohydrates on hemagglutination were compared. Several protein fractions inhibited *E. coli* binding to erythrocytes; none of the lipids tested were inhibitory, and 2 lipids (phosphatidylcholine and cholesterol) appeared to stimulate binding. Of the sugars tested, only .alpha.-Me-D-glucoside and D-glucose inhibited hemagglutination. The implications of these observations with respect to the properties of the adhesin receptor on the erythrocyte membrane are discussed.  
 CC 14-3 (Mammalian Pathological Biochemistry)  
 IT Receptors  
 RL: PROC (Process)  
 (for *Escherichia coli* **mannose**-resistant adhesin, of erythrocytes of humans, characterization of)  
 IT *Escherichia coli*  
 (**mannose**-resistant adhesins of, human erythrocyte receptors for)  
 IT Erythrocyte  
 (*Escherichia coli* **mannose**-resistant adhesin **receptors** of, of human, characterization of)  
 IT Agglutinins and Lectins  
 RL: BIOL (Biological study)  
 (adhesive factors, **mannose**-resistant, human erythrocyte receptors for, of *Escherichia coli*)  
 IT 57-88-5, biological studies 9001-67-6 9026-00-0  
 RL: BIOL (Biological study)  
 (*Escherichia coli* binding by erythrocyte of human stimulation by, adhesins in relation to)

L35 ANSWER 1 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 2000:65106 HCPLUS  
 DOCUMENT NUMBER: 132:217431  
 TITLE: Prostaglandin E1 influences serum **cholesterol esterase** and lipase activity in different ways  
 AUTHOR(S): Pioruncka-Stolzmann, M.  
 CORPORATE SOURCE: Clinical Biochemistry, Department of General Chemistry, Karol Marcinkowski University of Medical Sciences, Poznan, Pol.  
 SOURCE: Int. J. Tissue React. (1999), 21(3), 79-83  
 CODEN: IJTEDP; ISSN: 0250-0868  
 PUBLISHER: Bioscience Ediprint Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The in vitro and in vivo effects of prostaglandin E1 on cholesterol ester hydrolase (CEase) and lipase [glycerol ester hydrolase (GEH)] activity in human serum were examd. Cholesterol esterase and lipase activity in the sera of men with atherosclerosis differed substantially from that in the control subjects. CEase activity was raised and GEH activity suppressed in the serum of men with atherosclerosis compared with controls. Prostaglandin E1 in vitro was found to suppress lipase but to increase cholesterol esterase activity to some extent. However, in vivo activities of GEH and CEase in the sera of men with chronic arterial occlusions of the lower limbs treated with prostaglandin E1 revealed that lipase activity was increased but that cholesterol esterase activity was unchanged. Recent studies have demonstrated that by altering the metabolic pathways of acylcholesterols and triacylglycerols, prostaglandin E1 may lead to the development of new strategies for retarding atherosclerosis.

REFERENCE COUNT: 15  
 REFERENCE(S):  
 (1) Aviram, M; J Biol Chem 1991, V266, P11567 HCPLUS  
 (2) Brodt-Eppley, J; Biochim Biophys Acta 1995, V1272,  
     P69 HCPLUS  
 (4) Hajjar, D; Biochem Pharmacol 1985, V34, P295  
     HCPLUS  
 (5) Hajjar, D; J Lipid Res 1983, V24, P1176 HCPLUS  
 (6) Khoo, J; J Biol Chem 1981, V256, P12659 HCPLUS  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 2 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1999:335143 HCPLUS  
 DOCUMENT NUMBER: 131:128039  
 TITLE: Relationship of human pancreatic cholesterol esterase gene structure with lipid phenotypes  
 AUTHOR(S): Aleman-Gomez, Jose A.; Colwell, Niall S.; Vyas, Kamlesh; Boreck, Ingrid; Shonfeld, Gustav; Lange, Louis G.; Kumar, Vijaya B.  
 CORPORATE SOURCE: Department of Medicine, Washington University Medical Center, St. Louis, MO, USA  
 SOURCE: Life Sci. (1999), 64(25), 2419-2427  
 CODEN: LIFSAK; ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Pancreatic cholesterol esterase is one of the enzymes that plays a pivotal role in cholesterol absorption. Differences in the genotype of this enzyme could affect the susceptibility of individuals to dyslipidemia and/or cardiovascular disease. We undertook this study to investigate if any correlation exists between restriction fragment length polymorphism in the human pancreatic cholesterol esterase gene and serum lipid levels. DNA from 96 healthy adults was restricted with Stu I, Southern blotted, and probed with cDNA of human pancreatic cholesterol esterase. Results revealed six distinct patterns which were classified as A, B, C, D, E, and F which had a population frequency of 1%, 34.5%, 49%, 12.5%, 1% and 2% resp. Correlation of the distribution of lipid and lipoprotein levels by pattern and sex revealed a significant interaction between pattern type and HDL ( $p=0.03$ ) in the most common group (group C) for males. Male patients of pattern C tended to have a lower LDL cholesterol than non-pattern C males ( $p=0.07$ ); in addn., 80% of all males in the study population with LDL cholesterol under 100 mg/dL were found in pattern C. Thus, the most common Stu I RFLP genotype is assocd. with a favorable lipid phenotype. This report shows an assocn. between the human pancreatic cholesterol esterase genotype and serum lipid levels. Further anal. of a larger study group with Stu I and alternative polymorphic restriction enzymes is warranted, to confirm this biol. plausible result.

REFERENCE COUNT: 32  
 REFERENCE(S): (1) Bosner, M; Proc Natl Acad Sci USA 1988, V85, P7438

HCAPLUS

- (2) Brodt-Eppley, J; Biochim Biophys Acta 1995, V1272, P69 HCAPLUS
- (3) Brodt-Eppley, J; Journal of Lipid Research 1994, V35, P27 HCAPLUS
- (5) Cooper, D; Human Genetics 1984, V66, P1 HCAPLUS
- (7) Fontaine, R; Biochemistry 1991, V30, P7008 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L35 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1999:190911 HCAPLUS  
 DOCUMENT NUMBER: 130:336263  
 TITLE: Paradoxical effect on atherosclerosis of  
 hormone-sensitive lipase overexpression in macrophages  
 Escary, Jean-Louis; Choy, Henry A.; Reue, Karen; Wang,  
 Xu-Ping; Castellani, Lawrence W.; Glass, Christopher  
 K.; Lusis, Aldons J.; Schotz, Michael C.  
 CORPORATE SOURCE: Lipid Research Laboratory, West Los Angeles VA Medical  
 Center, Los Angeles, CA, 90073, USA  
 SOURCE: J. Lipid Res. (1999), 40(3), 397-404  
 CODEN: JLPRAW; ISSN: 0022-2275  
 PUBLISHER: Lipid Research, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Foam cells formed from receptor-mediated uptake of lipoprotein cholesterol by macrophages in the arterial intima are crit. in the initiation, progression, and stability of atherosclerotic lesions. Macrophages accumulate cholesterol when conditions favor esterification by acyl-CoA:cholesterol acyltransferase (ACAT) over cholestryl-ester hydrolysis by a neutral cholestryl-ester hydrolase, such as hormone-sensitive lipase (HSL), and subsequent cholesterol efflux mediated by extracellular acceptors. The authors recently made stable transfectants of a murine macrophage cell line, RAW 264.7, that overexpressed a rat HSL cDNA and had a 5-fold higher rate of cholestryl-ester hydrolysis than control cells. The current study exampd. the effect of macrophage-specific HSL overexpression on susceptibility to diet-induced atherosclerosis in mice. A transgenic line overexpressing the rat HSL cDNA regulated with a macrophage-specific scavenger receptor promoter-enhancer was established by breeding with C57BL/6J mice. Transgenic peritoneal macrophages exhibited macrophage-specific 7-fold overexpression of HSL cholesterol esterase activity. Total plasma cholesterol levels in transgenic mice fed a chow diet were modestly elevated 16% compared to control littermates. After 14 wk on a high-fat, high-cholesterol diet, total cholesterol increased 3-fold, with no difference between transgenics and controls. However, HSL overexpression resulted in thicker aortic fatty lesions that were 2.5-times larger in transgenic mice. HSL expression in the aortic lesions was shown by immunocytochem. Atherosclerosis was more advanced in transgenic mice exhibiting raised lesions involving the aortic wall, along with lipid accumulation in coronary arteries occurring only in transgenics. Thus, increasing cholestryl-ester hydrolysis, without concomitantly decreasing ACAT activity or increasing cholesterol efflux, is not sufficient to protect against atherosclerosis.

REFERENCE COUNT: 27  
 REFERENCE(S):

- (1) Beisiegel, U; Curr Opin Lipidol 1996, V7, P265 HCAPLUS
- (2) Bernard, D; J Biol Chem 1991, V266, P710 HCAPLUS
- (3) Bocan, T; Arterioscler Thromb 1991, V11, P1830 HCAPLUS
- (4) Brown, M; J Biol Chem 1980, V255, P9344 HCAPLUS
- (6) Cheng, D; J Biol Chem 1995, V270, P685 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

Ozga 09/775,517

L35 ANSWER 4 OF 14 HCPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 1996:443934 HCPLUS  
DOCUMENT NUMBER: 125:109649  
TITLE: Chromatographic separation and analysis of serum remnant-like lipoproteins  
INVENTOR(S): Kitamura, Takashi; Kato, Yoshio; Okazaki, Myo;  
Sasamoto, Keiko  
PATENT ASSIGNEE(S): Tosoh Corp, Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08105876	A2	19960423	JP 1994-215768	19940909
			JP 1994-190511	19940812

PRIORITY APPLN. INFO.: AB Serum remnant-like lipoproteins is sepd. by chromatog. column and the cholesterol content in the sepd. chylomicrons and VLDL is detd. by enzyme bioassay. The disclosed method allows automation of the anal. possible. TSKgel Lipopropak column was used for sepn. Enzyme, such as cholesterol esterase, cholesterol oxidase and/or peroxidase, and quinone dye, such as N-ethyl-N-(3-methylphenyl)-N'-succinylethylenediamine, N-ethyl-N-(3-sulfopropyl)-m-anisidine or 4-aminoantipyrine, are used for cholesterol detn.

L35 ANSWER 5 OF 14 HCPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 1996:443933 HCPLUS  
DOCUMENT NUMBER: 125:81273  
TITLE: Antibody-containing packing material for separating lipoproteins  
INVENTOR(S): Kitamura, Takashi; Kato, Yoshio; Okazaki, Myo;  
Sasamoto, Keiko  
PATENT ASSIGNEE(S): Tosoh Corp, Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08105875	A2	19960423	JP 1994-215767	19940909
			JP 1994-190510	19940812

PRIORITY APPLN. INFO.: AB Chromatog. column filled with packing material contg. immobilized monoclonal anti-human apoA-1 and anti-human apoB-100 antibodies that do not recognizing apo-B-48 is disclosed for sepg. remnant-like lipoproteins for cholesterol detn. Enzyme, such as cholesterol esterase, cholesterol oxidase and/or peroxidase, and quinone dye, such as N-ethyl-N-(3-methylphenyl)-N'-succinylethylenediamine, N-ethyl-N-(3-sulfopropyl)-m-anisidine or 4-aminoantipyrine, are used for cholesterol detn.

L35 ANSWER 6 OF 14 HCPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 1996:58448 HCPLUS  
DOCUMENT NUMBER: 124:199374  
TITLE: Impaired mobilisation of cholesterol from stored cholestrylo esters in human (THP-1) macrophages  
AUTHOR(S): Graham, Annette; Angell, Anthony D. R.; Jepson, Catherine A.; Yeaman, Stephen J.; Hassall, David G.  
CORPORATE SOURCE: Biology Division, Wellcome Research Laboratories,

SOURCE: Langley Court, Beckenham Kent, BR3 3BS, UK  
 Atherosclerosis (Shannon, Irel.) (1996), 120(1,2),  
 135-45  
 CODEN: ATHSBL; ISSN: 0021-9150

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The formation of macrophage-derived foam cells is central to the development of fatty streaks within the arterial wall, and to the progression of atherosclerosis. The unregulated deposition of cholestryl esters, as lipid droplets within the cytoplasm of these cells, is responsible for the formation of foam cells; this process is thought to be regulated by the balance between cholesterol esterification, by acyl CoA:cholesterol acyltransferase (ACAT), and hydrolysis, by neutral cholestryl ester hydrolase (nCEH). This study examines the importance of the balance between these two enzymes in detg. the efflux of cholesterol from human (THP-1) macrophages. The presence of modified lipoprotein, or of 25-hydroxycholesterol, markedly increased cholesterol esterification in these cells and these effects were potently inhibited by the presence of the ACAT inhibitor, 447C88. In the absence of HDL, an acceptor particle, there was little or no hydrolysis of the cholestryl ester pool and no efflux of cholesterol to the extracellular milieu; addn. of HDL led to a partial (36%) redn. in cholestryl esters, an effect which was not enhanced by the inhibition of ACAT. This suggested that the stored cholestryl esters in human (THP-1) macrophages, unlike those in mouse peritoneal macrophages, were relatively resistant to removal by efflux to HDL. Efflux of newly synthesized free cholesterol from these macrophages was increased by HDL in a saturable manner, suggesting that the lack of redn. of stored cholestryl esters was due to impaired mobilisation of cholestryl esters to free cholesterol via nCEH. Indeed, nCEH activity in these macrophages was much lower than in mouse peritoneal macrophages, and appeared to be down-regulated in the presence of 25-hydroxycholesterol or modified lipoproteins; this loss of nCEH activity was prevented by the ACAT inhibitor 447C88. The efflux of stored cholestryl esters from THP-1 macrophages therefore appears to be limited by the activity of nCEH.

L35 ANSWER 7 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1994:190360 HCPLUS  
 DOCUMENT NUMBER: 120:190360  
 TITLE: Protamine as an inhibitor for pancreatic lipase and cholesterol esterase and its use as food additive  
 INVENTOR(S): Okuda, Hiromichi  
 PATENT ASSIGNEE(S): Suisancho Chokan, Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05339168	A2	19931221	JP 1992-147760	19920608

AB Pancreatic lipase and cholesterol esterase inhibitors, which delay absorption of dietary fats and cholesterol from the intestine, contain protamine as an active ingredient. The inhibitors prevent hyperlipidemia and arteriosclerosis. Herring protamine at .gtoreq.1 .mu.g/mL inhibited activity of pancreatic lipase on triolein.

L35 ANSWER 8 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1992:548339 HCPLUS  
 DOCUMENT NUMBER: 117:148339  
 TITLE: Comparative studies on acid cholesterol

Ozga 09/775, 517

**AUTHOR(S):** esterase in renal blood vessels and aorta of control and hypercholesterolemic rabbits  
**CORPORATE SOURCE:** Kamanna, Vaijinath S.; Vora, Sanjay; Roh, Daeyoung;  
**SOURCE:** Kirschenbaum, Michael A.  
**DOCUMENT TYPE:** Dep. Med., Univ. California, Long Beach, CA, USA  
**LANGUAGE:** Atherosclerosis (Shannon, Irel.) (1992), 94(1), 27-33  
**AB** Journal  
**AB** CODEN: ATHSBL; ISSN: 0021-9150  
Decreased acid cholesterol esterase has been linked to cholesteryl ester accumulation and development of atherosclerosis. The cholesterol esterase activity was compared with the accumulation of cholesterol and its esters in the aorta, renal artery, and renal preglomerular microvessels of rabbits fed a 2% cholesterol diet for 1 mo. The cholesterol esterase activity was increased in microvessels from cholesterol-fed animals compared to the activities in the aorta and renal artery. Cholesterol feeding increased the cholesterol and cholesteryl ester accumulation in all vascular tissues. The percent distribution of esterified/total cholesterol in renal microvessels was decreased, consistent with the concomitant increases in cholesterol esterase activities. The aorta and renal artery exhibited an increase in cholesterol and cholesteryl ester accumulation and an increase in the percent of esterified cholesterol, consistent with a decrease in acid cholesterol esterase after cholesterol feeding. Renal microvessels, compared to the aorta and renal artery, may be relatively protected from developing atherosclerotic microvascular lesions by an organ-specific increase in acid cholesterol esterase activity.

L35 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 1991:59820 HCAPLUS  
DOCUMENT NUMBER: 114:59820  
TITLE: Activity of lysosomal hydrolases in various rabbit tissues in experimental atherosclerosis  
AUTHOR(S): Tabagari, S. I.; Feofilaktova, S. N.; Varsanovich, E. A.; Vasil'ev, A. V.; Tutelyan, V. A.  
COPORATE SOURCE: Inst. Nutr., Moscow, USSR  
SOURCE: Vopr. Med. Khim. (1990), 36(6), 32-4  
CODEN: VMDKAM; ISSN: 0042-8809  
DOCUMENT TYPE: Journal  
LANGUAGE: Russian  
**AB** The activity of cathepsins D, B, C, H, L, acid lipase, acid cholesterol ester hydrolase, phospholipases A1, A2, and glucuronidase were studied in the liver, small intestinal mucosa, intimal aortic cells, blood platelets, and monocytes of rabbits after oral administration of cholesterol at daily doses of 300 mg/kg for 100 days. Distinct changes in the functional state of lysosomal systems were found in the liver, monocytes and aortic intima cells. Possible mechanisms of the obsd. enzymol. changes are discussed.

L35 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 1988:404710 HCAPLUS  
DOCUMENT NUMBER: 109:4710  
TITLE: Lysosomal enzyme activity of monocytes/macrophages after incubation with postprandial hyperlipidemic serum and its role in atherogenesis  
AUTHOR(S): Henze, K.; Wolfram, G.  
COPORATE SOURCE: Med. Poliklin., Univ. Muenchen, Munich, Fed. Rep. Ger.  
SOURCE: Klin. Wochenschr. (1988), 66(4), 144-8  
CODEN: KLWOAZ; ISSN: 0023-2173  
DOCUMENT TYPE: Journal  
LANGUAGE: German  
**AB** Monocytes were obtained from the blood of healthy human volunteers and incubated for 24 h in RPMI 1640 medium + 30% homologous serum. Then the cells were incubated for an addnl. 24 h in either (1) homologous

hyperlipidemic serum obtained within 2 h of ingesting a fatty meal or (2) homologous normal serum obtained after an overnight fast of at least 12 h duration. Monocytes incubated in hyperlipidemic serum contained lower activities of lysosomal enzymes (cathepsin B, acid cholesteryl ester hydrolase, and N-acetyl-beta-D-glucosaminidase) than those incubated in normal, overnight serum. The relevance of this finding to the development of foam cells from macrophages in atherogenesis is discussed.

L35 ANSWER 11 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1986:440335 HCPLUS  
 DOCUMENT NUMBER: 105:40335  
 TITLE: Herpesvirus infection prevents activation of cytoplasmic cholesteryl esterase in arterial smooth muscle cells  
 AUTHOR(S): Hajjar, David P.  
 CORPORATE SOURCE: Cornell Med. Cent., New York Hosp., New York, NY, 10021, USA  
 SOURCE: J. Biol. Chem. (1986), 261(17), 7611-14  
 CODEN: JBCHA3; ISSN: 0021-9258  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Herpesvirus infection has previously been shown to alter the cholesteryl ester cycle in avian arterial smooth muscle cells, resulting in cytoplasmic cholesteryl ester accumulation. This study attempted to define some of the regulatory mechanisms assocd. with the control of cytoplasmic cholesteryl esterase in Marek's disease herpesvirus (MDV)-infected cells. Cholesteryl esterase activity in MDV-infected cells could not be activated by 1) dibutyryl cAMP, 2) dibutyryl cAMP added together with protein kinase, or 3) agonists of adenylate cyclase. Activation of cytoplasmic cholesteryl esterase activity occurred in uninfected cells and in cells infected with a control virus, turkey herpesvirus. The rate of cholesterol efflux from arterial smooth muscle cells challenged with dibutyryl cAMP was unchanged in MDV-infected cells as compared to uninfected or turkey herpesvirus-infected cells in which efflux was increased. It is proposed that the reduced cytoplasmic cholesteryl esterase activity in lipid-laden, herpesvirus-infected cells is due partly to its inability to be activated by the cAMP-protein kinase mechanism. This may contribute to the pathol. changes seen in MDV-infected arterial cells, including accumulation of intracellular cholesteryl esters.

L35 ANSWER 12 OF 14 HCPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1986:66861 HCPLUS  
 DOCUMENT NUMBER: 104:66861  
 TITLE: Virus-induced atherosclerosis. Herpesvirus infection alters aortic cholesterol metabolism and accumulation  
 AUTHOR(S): Hajjar, David P.; Fabricant, Catherine G.; Minick, C. Richard; Fabricant, Julius  
 CORPORATE SOURCE: Cornell Med. Cent., New York Hosp., New York, NY, 10021, USA  
 SOURCE: Am. J. Pathol. (1986), 122(1), 62-70  
 CODEN: AJPA4; ISSN: 0002-9440  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The effect of Marek's disease herpesvirus (MDV) infection on aortic cholesterol and cholesteryl ester (CE) metab. was studied. At 4 and 8 mo of age after MDV inoculation, MDV-infected animals had a significant 2-3-fold increase in total aortic lipid accumulation, characterized by significant increases in cholesterol, CE, triacylglycerol, and phospholipid, as compared with aortas from uninfected animals. At 8 mo of age, similar increases in aortic lipid accumulation were obsd. in MDV-infected animals as compared with those animals vaccinated with turkey

herpesvirus and later challenged with MDV. CE synthetic activity was increased significantly by 50% at 4 mo of age in the MDV-infected group as compared with the uninfected group, which could explain the initial increase in CE accumulation. By 8 mo of age, 2-fold increase in CE synthetic activity and a 30% and 80% redn. in lysosomal and cytoplasmic CE hydrolytic activities resp., were obsd. in aortas of MDV-infected chickens. Moreover, infection with MDV blocked the activation of cytoplasmic CE hydrolytic activity by dibutyryl cAMP or exogenous cAMP-dependent protein kinase. Apparently, lipid accretion in aortas of MDV-infected chickens results, in part, from alterations in cholesterol/CE metab. during early stages of the disease. Human atherosclerosis may result from specific herpesvirus infection which can alter lipid metab. and lead to lipid accretion.

L35 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1985:420666 HCAPLUS  
 DOCUMENT NUMBER: 103:20666  
 TITLE: Altered cholesterol ester cycle is associated with lipid accumulation in herpesvirus-infected arterial smooth muscle cells  
 AUTHOR(S): Hajjar, David P.; Falcone, Domenick J.; Fabricant, Catherine G.; Fabricant, Julius  
 CORPORATE SOURCE: Med. Coll., Cornell Univ., New York, NY, 10021, USA  
 SOURCE: J. Biol. Chem. (1985), 260(10), 6124-8  
 CODEN: JBCHA3; ISSN: 0021-9258  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The effects of Marek's disease herpesvirus (MDV) on cholesterol and cholesterol ester metab. in cultured chicken arterial smooth muscle cells were studied. Infection of arterial smooth muscle cells from specific pathogen-free chickens with MDV, but not a virus control (herpesvirus of turkeys) led to a 7-10-fold increase in the accumulation of free and esterified cholesterol and a 2-fold increase in phospholipids. The cellular lipid changes obsd. in the MDV-infected arterial smooth muscle cells resulted, in part, from the following: decreased low-d. lipoprotein-cholesterol ester hydrolysis due to decreased lysosomal (acid) cholesterol ester hydrolytic activity; increased de novo synthesis of cholesterol; decreased excretion of free cholesterol; and both increased cholesterol ester synthetic activity and decreased cytoplasmic (neutral) cholesterol ester hydrolytic activity which resulted in increased incorporation of oleic acid into cholesterol ester. Other changes noted in the MDV-infected cells as compared to uninfected cells included a 2-fold increase in both total protein synthesis and lysosomal and microsomal marker enzyme activities. These alterations in lipid and protein metab. in MDV-infected arterial smooth muscle cells may explain in part the in vivo findings that MDV infection of specific pathogen-free chickens fed a normocholesterolemic diet will induce arterial thickening and lipid accumulation resembling human atherosclerosis.

L35 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1972:486398 HCAPLUS  
 DOCUMENT NUMBER: 77:86398  
 TITLE: Aortic lipolytic enzymes in atherosclerosis  
 AUTHOR(S): Howard, A. N.; Patelski, J.; Bowyer, D. E.; Gresham, G. A.  
 CORPORATE SOURCE: Dep. Invest. Med., Univ. Camb., Cambridge, Engl.  
 SOURCE: Biochem. J. (1972), 128(1), 41P  
 CODEN: BIJOAK  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Atherosclerotic baboons, fed on a hypercholesterolemic diet, showed an 80% increase in aortic lipase activity but normal cholesterol ester hydrolase activity. Compared with control animals, oleate and arachidonate were

Ozga 09/775,517

increased and linoleate decreased in the cholesteryl esters; arachidonate was increased and linoleate decreased in phosphatidylcholine. After a course of i.v. injections of polyunsatd. phosphatidylcholine (Lipostabil), aortic lipase activity was normal, but cholesteryl ester hydrolase activity was increased by 50%. The elevated cholesterol plasma concn., the concn. of phospholipids, and the fatty acid compns. of cholesteryl esters and phosphatidylcholine were unchanged. Lipostabil decreased aortic lipid deposition by its effect on lipolytic enzymes.

Ozga 09/775,517

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DEL HIS Y  
L1 225 S ESTERASE (2A) CHOLESTEROL? OR CHOLESTERASE# OR CHOLESTERIN ES  
L2 2 S LYSOSOMAL ACID LIPASE# OR STEROL (W) (ESTER HYDROLASE# OR EST  
L3 226 S L1 OR L2  
L4 7093 S ATHEROSCLEROSIS? OR ANTIARTERIOSCLER?  
L5 7168 S L4 OR ANTIATHEROSCLER?  
L6 7744 S L5 OR ATHEROSCLER?  
L7 26 S L3 AND L6  
L8 2 S LIPID HYDROLYZING (3A) (PROTEIN# OR POLYPEPTIDE# OR ENZYME?)  
L9 227 S L3 OR L8  
L10 26 S L9 AND L6

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ENTER DISPLAY FORMAT (STD):end

=> d .wp 1-26

L10 ANSWER 1 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 2001-476267 [51] WPIDS  
DNC C2001-142904  
TI Providing **lipid hydrolyzing protein** to  
deficient cells, used to reduce **atherosclerotic** plaques,  
comprises administering a vector comprising and expressing a DNA sequence  
encoding biologically active **lipid hydrolyzing**  
**protein**.  
DC B04 D16  
IN DU, H; GRABOWSKI, G A  
PA (CHIL-N) CHILDRENS HOSPITAL RES FOUND  
CYC 93  
PI WO 2001056596 A1 20010809 (200151)\* EN 61p  
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZW  
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM

DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC  
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE  
 SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

ADT WO 2001056596 A1 WO 2001-US3481 20010202

PRAI US 2001-180362 20010202; US 2000-180362 20000204

AB WO 200156596 A UPAB: 20010910

**NOVELTY** - Providing (M1) biologically active **lipid hydrolyzing protein** or **polypeptide** or their mixtures, to cells of a mammal deficient in biologically active **lipid hydrolyzing protein** or **polypeptide**, comprising administering into cells a vector comprising and expressing a DNA sequence encoding biologically active **lipid hydrolyzing protein** or **polypeptide**, and expressing the DNA sequence in the cells, is new.

**ACTIVITY** - **Antiarteriosclerotic**.

**MECHANISM OF ACTION** - The LAL degrades lipoprotein-associated lipids presented to the lysosome.

Every third day for 30 days, LAL was administered as an intravenous bolus via tail vein of lal-/- mice. The mice received a regular chow diet and LAL dosing was begun at 2 months of age. Doses of LAL were 1.48 U (21 micro g, 70 micro l) LAL in 1 x phosphate buffered saline (PBS) with 2 % human serum albumin (HSA) and 10 mM of dithiothreitol (DTT). Control groups received 1 x PBS with 2 % HSA and 10 mM of DTT.

Triglycerides from the liver, spleen, and small intestine were determined by chemical analyses: the triglyceride concentration in the treated group was 65 % reduced compared to the untreated group.

**USE** - M1 is used to reduce **atherosclerotic** plaques in the treatment of **atherosclerosis** (claimed), or to treat Wolman's Disease, or Cholesteryl Ester Storage Disease (claimed).

Dwg.0/4

L10 ANSWER 2 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1999-527033 [44] WPIDS  
 DNC C1999-154779  
 TI Preparation of 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester comprises carbonylation and coupling reaction, then carbonylation/hexylamine reaction, dealkylation and phenoxy carbonylation.

DC B03

IN JIRKOVSKY, I

PA (AMHP) AMERICAN HOME PROD CORP

CYC 1

PI US 5952506 A 19990914 (199944)\* 7p  
 ADT US 5952506 A Provisional US 1997-44805 19970424, US 1998-62515 19980417

PRAI US 1997-44805 19970424; US 1998-62515 19980417

AB US 5952506 A UPAB: 19991026

**NOVELTY** - Preparation of 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester comprises reacting piperidine-1-carboxylic acid 4-phenoxyphenyl ester with carbonylating agent and 1-benzyl- (or 1-methyl-) 4-hydroxypiperidine with carbonylating agent and 6-amino hexanol, followed by reaction with a carbonylating agent and hexylamine, followed by dealkylation and concomitant phenoxy carbonylation.

**DETAILED DESCRIPTION** - Preparation of 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)-piperidine-1-carboxylic acid 4-phenoxyphenyl ester (I) comprises:

(a) reacting 1-benzyl-4-hydroxypiperidine or 1-methyl-4-hydroxypiperidine in an aprotic solvent at 0-70 deg. C (optionally in the presence of a tertiary amine) with:

(i) a carbonylating coupling reagent selected from carbonyldiimidazole, disuccinimidyl carbonate, 2,2'-carbonyl-bis(3,5-dioxo-1,2,4-oxazolidine) or 3,3'-carbonyl bis(5-phenyl-1,3-1,3,4-oxadiazole-2(3H)thione) and;

(ii) 6-amino hexanol;  
 (b) reacting the resultant 4-((6-hydroxyhexyl)carbamoyloxy)piperidine

derivative in an aprotic solvent at 0-70 deg. C (optionally in the presence of a tertiary amine) with:

(i) a carbonylating coupling reagent as above; and

(ii) hexylamine; and

(c) dealkylation and concomitant N-(4-phenoxy)phenoxy carbonylation of the intermediate 4-(6-(hexylcarbamoyloxy)hexylcarbamoyloxy)piperidine derivative with 4-phenoxyphenyl chloroformate in an aprotic solvent at 15-110 deg. C to give (I).

ACTIVITY - Antilipemic; antiarteriosclerotic.

MECHANISM OF ACTION - Sterol-Esterase-Inhibitor;

Sterol-O-Acyltransferase-Inhibitor; ACAT-Inhibitor.

USE - For the large-scale preparation of (I) (claimed). (I) is useful for reducing cholesterol absorption and in the treatment of hypercholesterolemia, hyperlipidemia and atherosclerosis.

ADVANTAGE - (I) inhibits cholesterol ester

hydrolase and acylcoenzyme A cholesterol acyltransferase. The preparation is carried out without isolation of intermediates and without changing solvents. The preparation gives improved purity, higher yields, lower costs, technical convenience and is less labor and time intensive than the prior art route in EP0635501-A1.

Dwg.0/0

L10 ANSWER 3 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1999-222370 [19] WPIDS  
 DNC C1999-065023  
 TI Manufacture of cholesterol esterase for estimation of esterified cholesterol in blood - by culturing microorganism belonging to Xanthomonas genus and having cholesterol esterase synthesizing ability followed by extraction of enzyme from culture.

DC B04 D16

PA (KIKK) KIKKOMAN CORP

CYC 1

PI JP 11056355 A 19990302 (199919)\* 14p

ADT JP 11056355 A JP 1997-239163 19970821

PRAI JP 1997-239163 19970821

AB JP 11056355 A UPAB: 19990518

NOVELTY - Microorganism belonging to Xanthomonas genus which has cholesterol esterase synthesizing ability is grown in a culture medium. The enzyme produced is extracted from the culture medium.

USE - As a reagent for estimation of esterified cholesterol in blood used for diagnosis of atherosclerosis, myocardial infarction etc.

ADVANTAGE - The enzyme has high thermal stability and is obtained easily.

Dwg.0/4

L10 ANSWER 4 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1998-609956 [51] WPIDS  
 DNC C1998-182788  
 TI 4-Carbamoyloxy-piperidine-1-carboxylate ester derivative preparation - in 3 stages from 4-hydroxy-piperidine derivative via new intermediates, used as cholesterol absorption inhibitor.

DC B03 B05

IN JIRKOVSKY, I

PA (AMHP) AMERICAN HOME PROD CORP

CYC 79

PI WO 9847870 A1 19981029 (199851)\* EN 14p

RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW

Ozga 09/775,517

ADT AU 9869469 A 19981113 (199913) 16p  
ZA 9803399 A 19991229 (200006)  
WO 9847870 A1 WO 1998-US6513 19980331; AU 9869469 A AU 1998-69469  
19980331; ZA 9803399 A ZA 1998-3399 19980422

FDT AU 9869469 A Based on WO 9847870  
PRAI US 1997-845565 19970424  
AB WO 9847870 A UPAB: 19981223

Preparation of 4-[(6-hexylcarbamoyloxy)-hexylcarbamoyl]piperidine-1-carboxylic acid 4-phenoxyphenyl ester (I) comprises: (a) reacting 1-(benzyl or methyl)-4-hydroxypiperidine (II) with a carbonylating coupling reagent and 6-aminohexanol (III) in an aprotic solvent at 0-70 deg. C, optionally in the presence of a tertiary amine; (b) reacting the resultant 1-(benzyl or methyl)-4-[(6-hydroxyhexyl)carbamoyloxy]-piperidine (IV) with hexylamine (V) under the conditions of step (1); and (c) dealkylation and concomitant N-(4-phenoxy)-phenoxy carbonylation of the intermediate 1-(benzyl or methyl)-4-[(6-hydroxyhexyl)carbamoyloxy]-hexylcarbamoyl piperidine (VI) with 4-phenoxyphenyl chloroformate (VII) in an aprotic solvent 15-110 deg. C. Also claimed are novel intermediates (IV), (VI) and (VII). Step (c) is also claimed as a separate process.

USE - (I), described in EP 635501, inhibits both cholesterol acyltransferase, resulting in a reduction of cholesterol absorption. Possible uses include treatment of hypercholesterolaemia, hyperlipidaemia and atherosclerosis.

ADVANTAGE - This method utilises a single solvent throughout, requires no purification of intermediates and is suitable for large-scale production. The yield and purity of (I) are higher than in the normal laboratory-scale synthesis and the method is much less labour intensive.

Dwg.0/0

L10 ANSWER 5 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 1998-467731 [40] WPIDS  
DNN N1998-364435 DNC C1998-141911  
TI Determination of skin cholesterol levels - by enzymatic reaction in vessel sealed to skin surface.

DC B04 D16 S03 LOPUKHIN, J M; PARFENOV, A S; LOPUKHIN YU, M  
IN (PARF-I) PARFENOV A S; (IMII-N) IMI INT MEDICAL INNOVATIONS INC; (LOPU-I)  
PA LOPUKHIN YU M; (LOPU-I) LOPUKHIN J M  
CYC 82 WO 9837424 A1 19980827 (199840)\* RU 16p  
PI RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA  
PT SD SE SZ UG ZW  
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE  
GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG  
MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG  
US UZ VN YU ZW

AU 9857846 A 19980909 (199905)  
EP 987553 A1 20000322 (200019) EN  
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

BR 9807594 A 20000222 (200024)  
RU 2130189 C1 19990510 (200026)  
ADT WO 9837424 A1 WO 1998-RU10 19980126; AU 9857846 A AU 1998-57846 19980126;  
EP 987553 A1 EP 1998-901608 19980126, WO 1998-RU10 19980126; BR 9807594 A  
BR 1998-7594 19980126, WO 1998-RU10 19980126; RU 2130189 C1 RU 1997-102570  
19970220

FDT AU 9857846 A Based on WO 9837424; EP 987553 A1 Based on WO 9837424; BR  
9807594 A Based on WO 9837424  
PRAI RU 1997-102570 19970220

AB WO 9837424 A UPAB: 19981008  
Determination of skin cholesterol levels comprises sealing an open-bottomed vessel by its base to the skin surface; adding a buffer solution (pH 6.8) containing 2.0-2.5 U cholesterol oxidase, 0.04-0.06 wt.%

sodium deoxycholate and 0.1-0.2 wt.% 3-(dodecyldimethyl ammonium)-propane sulphonate; determining the cholesterol concentration in the reaction mixture by measuring the hydrogen peroxide concentration, and calculating the cholesterol content of the skin from the determined cholesterol concentration.

The reaction mixture also contains 3-5 U **cholesterol esterase**. The hydrogen peroxide concentration is measured: (a) by spectrophotometry after adding a peroxidase and a [chromogenic] substrate; (b) by immersing an electrochemical sensor in the reaction mixture, or (c) by immersing a colorimetric indicator (strip) in the reaction mixture.

**USE** - The method is used for early diagnosis of **atherosclerosis** and for monitoring **atherosclerosis** therapy.

**ADVANTAGE** - The method is more specific, simpler, more broadly applicable and more accurate than prior art methods (cf. US 5489510).  
Dwg.3/3

L10 ANSWER 6 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1998-078841 [08] WPIDS  
 DNN N1998-063081 DNC C1998-026383  
 TI Determination of low density lipoprotein cholesterol - using sugar conjugates of **cholesterol esterase** and **cholesterol oxidase**.  
 DC B04 D16 S03  
 IN FUTATSUGI, M; TANAKA, I  
 PA (WAKP) WAKO PURE CHEM IND LTD; (WAKP) WAKO JUNYAKU KOGYO KK  
 CYC 27  
 PI EP 819765 A2 19980121 (199808)\* EN 15p  
 R: AL AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT RO SE  
 SI  
 JP 10080300 A 19980331 (199823) 12p  
 CA 2210783 A 19980118 (199827)  
 KR 98010429 A 19980430 (199915)  
 US 5879901 A 19990309 (199917)  
 ADT EP 819765 A2 EP 1997-112007 19970715; JP 10080300 A JP 1997-210099  
 19970718; CA 2210783 A CA 1997-2210783 19970717; KR 98010429 A KR  
 1997-32313 19970711; US 5879901 A US 1997-895879 19970717  
 PRAI JP 1996-207770 19960718  
 AB EP 819765 A UPAB: 19980223  
 Method for measuring the amount of low-density lipoprotein (LDL) cholesterol in a sample comprises:  
 (a) mixing the sample with a first reagent solution containing a buffer;  
 (b) measuring the optical density (OD1) of the mixture;  
 (c) adding a second reagent solution containing **cholesterol esterase** and **cholesterol oxidase**;  
 (d) measuring the optical density (OD2) of the mixture;  
 (e) subtracting a value obtained by multiplying OD1 with a correction factor from OD2 to obtain a value OD3, and  
 (f) comparing OD3 with a calibration curve.  
 The first and/or second reagent solutions contain a coupler, a developer and a peroxidase. The **cholesterol esterase** and/or **cholesterol oxidase** is in the form of a conjugate with a sugar compound.  
 Also claimed are the reagents used in the method above.  
**USE** - The process is used for the diagnosis of **atherosclerosis** and disorders of lipid metabolism.  
**ADVANTAGE** - The conjugated enzymes react specifically with LDL cholesterol and not with high density lipoprotein (HDL) cholesterol.  
 Dwg.0/4

DNC C1995-124690  
 TI New heterocyclic oxime-carbamate derivs. - used as **cholesterol ester hydrolase** inhibitors for reducing blood cholesterol level, e.g. for treating **atherosclerosis**.  
 DC B05  
 IN FELMAN, S W; JIRKOVSKY, I; MEMOLI, K A  
 PA (AMHP) AMERICAN HOME PROD CORP  
 CYC 1  
 PI US 5438056 A 19950801 (199536)\* 15p  
 ADT US 5438056 A US 1993-131820 19931005  
 PRAI US 1993-131820 19931005  
 AB US 5438056 A UPAB: 19950918  
 Heterocyclic oxime carbamates of formula (I) are new: R1, R2 = thienyl, naphthyl, phenyl (opt. substd. by halogen, OMe or di-(1-3C alkyl)-amino) or substd. furanonyl of formula (a): or CR1R2 = 5H-indeno-(1,2-b)pyridin-5-ylidene, 9H-xanthen-9-ylidene or 10,10-dioxo-9H-thianthen-9-ylidene; R3, R4 = H or 4-20C hydrocarbyl; or NR3R4 = 4-(R8)-piperidino; R5, R6 = 1-3C alkyl, 5-7C cycloalkyl or phenyl (opt. substd. by 1-5C alkyl or halogen); R7 = H or halogen; R8 = 1-3C alkyl.  
 USE - (I) inhibit **cholesterol ester hydrolase**, and are useful for lowering, blood cholesterol (claimed), and may be useful for treating e.g. **atherosclerosis**, familial hypercholesterolaemia and hyperlipaemia.  
 Dwg.0/0

L10 ANSWER 8 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1995-138961 [18] WPIDS  
 DNC C1995-064231  
 TI New di benzo-furanyl-alkyl-carbamate derivs. - are **cholesterol ester hydrolase** inhibitors for treating **atherosclerosis** etc..  
 DC B02  
 IN COMMONS, T J; MEWSHAW, R E; STRIKE, D P  
 PA (AMHP) AMERICAN HOME PROD CORP  
 CYC 1  
 PI US 5401769 A 19950328 (199518)\* 5p  
 ADT US 5401769 A US 1994-190402 19940202  
 PRAI US 1994-190402 19940202  
 AB US 5401769 A UPAB: 19950518  
 Dibenzofuranyl-N-alkyl carbamate derivs. of formula (I) are new: R1, R2 = H, F, Cl, Br, I, CF3, CN, NO2, 1-6C alkyl, 1-6C alkoxy, CO2H, 2-7C alkylcarbonyl, 2-7C alkylcarbonyloxy, 2-7C alkoxy carbonyl, 2-7C alkoxy carbonyloxy, mono- or di(1-6C alkyl)aminocarbonyl or mono- or di(1-6C alkyl)aminocarbonyloxy; R3 = H or 1-6C alkyl; R4 = 2-18C alkyl, 3-8C cycloalkyl, 1-6C alkyl or 7-18C phenylalkyl (opt. ring substd. by 1-6C alkyl, 1-6C alkoxy, halo, NO2, CN, CF3 or phenyl).  
 USE - (I) inhibit the absorption of cholesterol from the intestinal tract by inhibiting **cholesterol ester hydrolase** (CEH). They are therefore used to treat **atherosclerosis**, familial hypercholesterolaemia, and hyperlipidaemia.  
 Dwg.0/0

L10 ANSWER 9 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1995-053622 [08] WPIDS  
 DNC C1995-024413  
 TI New tris carbamic acid ester(s) are ACAT inhibitors - useful for treating e.g. **atherosclerosis**, familial hypercholesterolaemia and hyperlipaemia.  
 DC B03  
 IN COMMONS, T J; LACLAIR, C M; STRIKE, D P; COMMONS, T J W  
 PA (AMHP) AMERICAN HOME PROD CORP  
 CYC 29

PI EP 635501 A1 19950125 (199508)\* EN 35p  
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE  
 AU 9467520 A 19950202 (199513)  
 CA 2128116 A 19950122 (199516)  
 FI 9403441 A 19950122 (199516)  
 BR 9402852 A 19950404 (199520)  
 JP 07089934 A 19950404 (199522) 27p  
 NZ 264032 A 19951221 (199606)  
 ZA 9405214 A 19960327 (199619) 55p  
 HU 70942 T 19951128 (199733)  
 BR 1100752 A3 19980505 (199825)  
 SG 47596 A1 19980417 (199826)  
 IL 110302 A 19980615 (199836)  
 AU 692157 B 19980604 (199839)  
 HU 216790 B 19990830 (199940)  
 US 5952354 A 19990914 (199944)  
 RU 2130928 C1 19990527 (200027)  
 TW 369527 A 19990911 (200035)#

ADT EP 635501 A1 EP 1994-305305 19940719; AU 9467520 A AU 1994-67520 19940718;  
 CA 2128116 A CA 1994-2128116 19940715; FI 9403441 A FI 1994-3441 19940720;  
 BR 9402852 A BR 1994-2852 19940718; JP 07089934 A JP 1994-165075 19940718;  
 NZ 264032 A NZ 1994-264032 19940718; ZA 9405214 A ZA 1994-5214 19940715;  
 HU 70942 T HU 1994-2108 19940715; BR 1100752 A3 BR 1997-1100752 19970512;  
 SG 47596 A1 SG 1996-3025 19940719; IL 110302 A IL 1994-110302 19940713; AU  
 692157 B AU 1994-67520 19940718; HU 216790 B HU 1994-2108 19940715; US  
 5952354 A US 1993-95140 19930721; RU 2130928 C1 RU 1994-26296 19940715; TW  
 369527 A TW 1994-100154 19940110

FDT AU 692157 B Previous Publ. AU 9467520; HU 216790 B Previous Publ. HU 70942

PRAI US 1993-95140 19930721; TW 1994-100154 19940110

AB EP 635501 A UPAB: 19950602  
 Tris carbamic acid esters of 4 - 8 membered azacycloalkanols of formula (I) and their salts are new; p = 0 - 4, Z = -Ar<sub>1</sub>, -Ar<sub>1</sub>-Ar<sub>2</sub>-, -Ar<sub>1</sub>-O-Ar<sub>2</sub>, -Ar<sub>1</sub>-S-Ar<sub>2</sub>, -Ar<sub>1</sub>-O-C(O)-Ar<sub>2</sub>, -Ar<sub>1</sub>-C(O)-O-Ar<sub>2</sub>, -Ar<sub>1</sub>-C(O)-Ar<sub>2</sub>, -Ar<sub>1</sub>-(CH<sub>2</sub>)<sub>1-20</sub>-Ar<sub>2</sub>, -Ar<sub>1</sub>-(CH<sub>2</sub>)<sub>1-20</sub>-O-Ar<sub>2</sub>, -Ar<sub>1</sub>-O-(CH<sub>2</sub>)<sub>1-20</sub>-Ar<sub>2</sub>, -Ar<sub>1</sub>-(CR<sub>6</sub>=CR<sub>6</sub>)<sub>1-3</sub>-Ar<sub>2</sub>, -(CR<sub>6</sub>=CR<sub>6</sub>)<sub>1-3</sub>-Ar<sub>2</sub> or -Ar<sub>1</sub>-NR<sub>7</sub>-Ar<sub>2</sub>; R<sub>6</sub> = H or 1-8C alkyl; R<sub>7</sub> = H, 1-8C alkyl, 1-8C alkylcarbonyl or 1-8C alkoxy carbonyl; Ar<sub>1</sub>, alkyl; R<sub>8</sub> = Ph, naphthyl, furanyl, benzofuranyl, pyrazinyl, thieryl, benzothienyl, imidazolyl, benzoxazolyl, thiazolyl, benzthiazolyl, indenyl, indolyl, quinolinyl, benzotriazolyl, carbazolyl, benzimidazolyl or fluorenyl etc. (all opt. subst.). A = a bridging gp. selected from 1-20C hydrocarbyl opt. unsatd. with 1-6 sites of olefinic and/or acetylenic unsaturation, -(CH<sub>2</sub>)<sub>m</sub>-W-(CH<sub>2</sub>)<sub>n</sub>- or -(CH<sub>2</sub>)<sub>b</sub>-Y-(CH<sub>2</sub>)<sub>c</sub>-; m, n = 1 - 19; m + n = 2 - 20; W = -O-, -S- or NR<sub>14</sub>; R<sub>14</sub> = H, 1-20C alkyl, 1-20C alkylcarbonyl, 1-20C alkoxy carbonyl or benzyl; b, c = 0 - 20; b + c = 1 - 20, Y = phenylene, pyridinylene, naphthylene, pyrrolylene or a gp. of formula (ii) - (v) etc.; R<sub>15</sub> = H, 1-8C alkyl, 1-20C alkylcarbonyl, 1-20C alkoxy carbonyl or benzyl; R<sub>1</sub>, R<sub>2</sub> = H, 1-8C alkyl, 1-8C alkoxy, 1-8C alkylcarbonyl, OH, CN, 1-8C alkylcarbonyloxy or -(CH<sub>2</sub>)<sub>0-6</sub>-NR<sub>18</sub>R<sub>19</sub>; R<sub>18</sub> = 1-8C alkyl, 1-8C alkoxy carbonyl or 1-8C alkylcarbonyl; R<sub>19</sub> = H or 1-8C alkyl; R<sub>3</sub> = H, 1-8C alkyl or 7-15C arylalkyl; aryl = Ph opt. subst. by alkyl; R<sub>4</sub>, R<sub>5</sub> = H, 1-20C alkyl, 2-20C alkenyl, 3-10C cycloalkyl, 1-6C alkyl; R<sub>6</sub>, R<sub>7</sub> = H, 1-20C alkenyl, 1-20C alkylcarbonyl, 1-20C alkoxy carbonyl or benzyl; R<sub>21</sub> = H or 1-20C alkyl; USE - (I) inhibit absorption of cholesterol from the intestinal tract and inhibit enzymes **cholesterol ester hydrolase** (CEH) and acyl-CoA cholesterol acyltransferase (ACAT). (I) are useful for treating **atherosclerosis**, familial hypercholesterolaemia and hyperlipidaemia.  
 Dwg.0/0

DNC C1995-013640  
 TI New dibenzofuran yl esters of N-heterocyclic carboxylic acids - useful for reducing cholesterol uptake from intestinal tract.  
 DC B02  
 IN COMMONS, T J; STRIKE, D P  
 PA (AMHP) AMERICAN HOME PROD CORP  
 CYC 1  
 PI US 5373009 A 19941213 (199504)\* 4p  
 ADT US 5373009 A US 1994-190416 19940202  
 PRAI US 1994-190416 19940202  
 AB US 5373009 A UPAB: 19950201  
 Dibenzofuran derivs. of formula (I) are new: R1, R2 = halogen, CF<sub>3</sub>, CN, NO<sub>2</sub>, 1-6C alkyl, 1-6C alkoxy, COOH, 2-7C alkanoyl, 2-7C alkanoyloxy, 2-7C alkoxy carbonyl, mono- or di(1-6C alkyl)aminocarbonyl or mono- or di(1-6C alkyl)aminocarbonyloxy; m, n and p = 0-2; R3 = 1-6C alkyl; X = O, S or CR<sub>4</sub>R<sub>5</sub>; R4, R5 = H or 1-6C alkyl, or CR<sub>4</sub>R<sub>5</sub> = 3-8C carbocyclic ring. Also claimed is a method of reducing cholesterol uptake from the intestinal tract by admin. of (I).

USE - (I) are **cholesterol ester hydrolase** (CEH) inhibitors for reducing cholesterol uptake from the intestinal tract. They may be used to treat e.g. **atherosclerosis**, familial hypercholesterolaemia, hyperlipaemia. (I) may be administered orally or parenterally

Dwg.0/0

L10 ANSWER 11 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1994-191540 [23] WPIDS  
 CR 1992-415936 [50]  
 DNN N1994-150710 DNC C1994-087622  
 TI Assay or isolation of lipoprotein (a) - using a lectin attached to a solid support to specifically bind lipoprotein (a) in a liq. sample.  
 DC B04 D16 S03  
 IN SEMAN, L J  
 PA (SEMA-I) SEMAN L J  
 CYC 1  
 PI US 5320968 A 19940614 (199423)\* 7p  
 ADT US 5320968 A CIP of US 1991-704457 19910523, US 1993-21189 19930223  
 PRAI US 1991-704457 19910523; US 1993-21189 19930223  
 AB US 5320968 A UPAB: 19940727  
 Assaying for lipoprotein (a) in a liq. sample contg. one or more other serum lipoproteins and having a pH of 6.9-7.5, comprises (a) contacting the liq. sample with a solid support reagent contg. lectin attached to a solid support to bind lipoprotein (a) to the support-bound lectin, (b) removing lipoproteins in the sample which are not bound to the support and (c) assaying the lipoprotein (a) remaining.

The lectin may be e.g. wheat germ agglutinin (WGA), lima bean agglutinins, phytohaemagglutinin or horseshoe crab lectins. The assay for cholesterol may comprise treating the lipoprotein (a) with **cholesterol esterase** and a surfactant to release cholesterol and reacting the released cholesterol with cholesterol oxidase to produce H<sub>2</sub>O<sub>2</sub> and assaying for H<sub>2</sub>O<sub>2</sub> using a peroxidase enzyme.

USE/ADVANTAGE - The assays can be used for detecting elevated lipoprotein (a) levels in subjects with coronary artery disease or **atherosclerosis**. The purified lipoprotein (a) can be used for the prodn. of antibodies. The lectin binds specifically to lipoprotein (a) and allows specific assay and isolation. The methods can provide a direct lipoprotein (a) determin. and have a margin of error of +/- 1%.

Dwg.0/3

L10 ANSWER 12 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1993-214331 [26] WPIDS  
 CR 1995-178125 [23]  
 DNN N1993-164702 DNC C1993-095146

TI Rapid, direct determinn. of low density lipoprotein - by pptn. in presence  
 of nucleating agent, removal of other lipoprotein(s), redissolution of  
 ppt. and assay.  
 DC A89 B04 S03  
 IN ERTINGSHAUSEN, G; LAW, W T; LAW, W; ERTINGHAUSEN, G  
 PA (ACTI-N) ACTIMED LAB INC  
 CYC 22  
 PI WO 9312429 A1 19930624 (199326)\* EN 25p  
 AU 9332796 A 19930719 (199344)  
 US 5286626 A 19940215 (199407) 5p  
 NO 9402197 A 19940610 (199430)  
 FI 9402763 A 19940610 (199431)  
 EP 619885 A1 19941019 (199440) EN  
 JP 07501945 W 19950302 (199517)  
 AU 661097 B 19950713 (199535)  
 EP 619885 B1 19961002 (199644) EN 12p  
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE  
 DE 69214297 E 19961107 (199650)  
 ADT WO 9312429 A1 WO 1992-US10809 19921211; AU 9332796 A AU 1993-32796  
 19921211; US 5286626 A US 1991-806183 19911213; NO 9402197 A WO  
 1992-US10809 19921211, NO 1994-2197 19940610; FI 9402763 A WO 1992-US10809  
 19921211, FI 1994-2763 19940610; EP 619885 A1 WO 1992-US10809 19921211, EP  
 1993-901285 19921211; JP 07501945 W WO 1992-US10809 19921211, JP  
 1993-511132 19921211; AU 661097 B AU 1993-32796 19921211; EP 619885 B1 WO  
 1992-US10809 19921211, EP 1993-901285 19921211; DE 69214297 E DE  
 1992-614297 19921211, WO 1992-US10809 19921211, EP 1993-901285 19921211  
 FDT AU 9332796 A Based on WO 9312429; EP 619885 A1 Based on WO 9312429; JP  
 07501945 W Based on WO 9312429; AU 661097 B Previous Publ. AU 9332796,  
 Based on WO 9312429; EP 619885 B1 Based on WO 9312429; DE 69214297 E Based  
 on EP 619885, Based on WO 9312429  
 PRAI US 1991-806183 19911213  
 AB WO 9312429 A UPAB: 19950626  
 Direct determinn. of low density lipoprotein (LDL) in a fluid comprises (1)  
 adding a polyanionic cpd. (I), divalent metal salt (II) and nucleating  
 agent (III) to the sample to form clusters of LDL; (2) adding enzymes to  
 destroy high and very low density lipoproteins selectively; (3)  
 redissolving the LDL and (4) determining its concn. conventionally.  
 Pref., (I) is dextran sulphate; heparin; phosphotungstic acid or  
 poly(vinyl sulphate). (II) is a Ca, Mn or Mg salt and (III) is porous Fe  
 oxide (opt. having (I) coated on it).  
 LDL is detected enzymatically after redissolution in EDTA-NaCl (esp.  
 a soln. of 2.5-6% NaCl and 0.05-0.1% EDTA); protease (75-100 units per  
 test) or MgCl<sub>2</sub> (50-200mM). Redissolved LDL is pref. reacted with  
 cholesterol oxidase (CO) and CE, and the H<sub>2</sub>O<sub>2</sub> formed determined  
 colorimetrically.  
 USE/ADVANTAGE - Provides a simple, sensitive and reliable determinn. of  
 LDL, usually within 2 min., (III) ensures rapid pptn. of LDL in a form  
 which is stable against surfactants and **cholesterol esterase** (CE).  
 Dwg.1/2  
 Dwg.1/2  
 Dwg.1/2  
 L10 ANSWER 13 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1992-432990 [52] WPIDS  
 DNC C1992-192232  
 TI New 1-piperidine carboxylic acid 4-phenoxyphenyl ester derivs. - are CEH  
 and ACAT inhibitors for treating hypercholesterolaemia, hyperlipaemia,  
 coronary heart disease and **atherosclerosis**.  
 DC B03  
 IN COMMONS, T J; STRIKE, D P  
 PA (AMHP) AMERICAN HOME PROD CORP  
 CYC 39

PI US 5169844 A 19921208 (199252)\* 10p  
 WO 9313067 A1 19930708 (199328) EN 28p  
 RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE  
 W: AU BB BG BR CA CS FI HU JP KP KR LK MG MN MW NO NZ PL RO RU SD  
 AU 9334251 A 19930728 (199347)  
 ADT US 5169844 A US 1991-812512 19911220; WO 9313067 A1 WO 1992-US11287  
 19921210; AU 9334251 A AU 1993-34251 19921210  
 FDT AU 9334251 A Based on WO 9313067  
 PRAI US 1991-812512 19911220  
 AB US 5169844 A UPAB: 19931118  
 Phenoxyphenyl 1-piperidinecarboxylate derivs. of formula (I) are new. In  
 (I) R1 = H, 1-20C alkyl, 3-20C alkenyl, 3-8C cycloalkyl, 3-8C  
 cycloalkyl-(1-6C)alkyl, phenyl (opt. substd. by 1-6C alkyl, 1-6C alkoxy,  
 halo, NO<sub>2</sub>, CN or CF<sub>3</sub>) or phenyl-(1-20C) alkyl (opt. ring substd. by 1-6C  
 alkyl, 1-6C alkoxy, halo, NO<sub>2</sub>, CN, CF<sub>3</sub> or Ph); R2 = H or 1-6C alkyl; or  
 NR1R2 forms a gp. of formula (a): n = 0-2; X = O, S or CR<sub>7</sub>R<sub>8</sub>; R7 = H, OH,  
 1-6C alkyl, 2-6C alkanoyloxy, 1-6C hydroxyalkyl, COOH, 1-16C  
 alkoxy carbonyl(sic) or phenyl (opt. substd. by 1-6C alkyl, 1-6C haloalkyl,  
 1-6C perhaloalkyl, halo, NO<sub>2</sub> or CN); R8 = H or 1-6C alkyl; or R7+R8  
 completes a 3-7C polymethylene ring; R9 = H, 1-6C alkyl or 2-12C gem  
 dialkyl; R3-R6 = H, 1-6C alkyl, 1-6C alkoxy, halo, NO<sub>2</sub>, CN, 1-6C  
 perhaloalkyl, 1-16C alkoxy carbonyl(sic) or COOH.  
 USE - (I) inhibit cholesterol ester hydrolose (CEH) and/or acyl  
 coenzyme A:cholesterol acyltransferase (ACAT) and so inhibit the formation  
 of cholestryl esters. Thus (I) interfere with, and prevent, assimilation  
 of cholesterol into the lymphatic system and thus the bloodstream. (I) can  
 be used to treat high serum cholesterol levels and associated diseases  
 (e.g., coronary heart disease, **atherosclerosis**, familiar  
 hypercholesterolaemia and hyperlipaemia).  
 0/0  
 Dwg.0/0

L10 ANSWER 14 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1992-415936 [50] WPIDS  
 CR 1994-191540 [23]  
 DNN N1992-317142 DNC C1992-184626  
 TI Assay for lipoprotein (A) in the presence of other lipoprotein(s) -  
 comprises using lectin attached to a solid support to selectively bind the  
 lipoprotein(A).  
 DC B04 S03  
 IN SEMAN, L J  
 PA (SEMAN-I) SEMAN L J  
 CYC 17  
 PI WO 9221015 A1 19921126 (199250)\* EN 23p  
 RW: AT BE CH DE DK ES FR GB GR IT LU MC NL SE  
 W: JP NO  
 EP 585387 A1 19940309 (199410) EN  
 R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE  
 EP 585387 A4 19950118 (199545)  
 EP 585387 B1 19990811 (199936) EN  
 R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE  
 DE 69229784 E 19990916 (199944)  
 ADT WO 9221015 A1 WO 1992-US4302 19920521; EP 585387 A1 EP 1992-913182  
 19920521, WO 1992-US4302 19920521; EP 585387 A4 EP 1992-913182 ;  
 EP 585387 B1 EP 1992-913182 19920521, WO 1992-US4302 19920521; DE 69229784  
 E DE 1992-629784 19920521, EP 1992-913182 19920521, WO 1992-US4302  
 19920521  
 FDT EP 585387 A1 Based on WO 9221015; EP 585387 B1 Based on WO 9221015; DE  
 69229784 E Based on EP 585387, Based on WO 9221015  
 PRAI US 1991-704457 19910523  
 AB WO 9221015 A UPAB: 19991026  
 A method is claimed for assaying lipoprotein (a) (LPA) in a liq. sample  
 contg. one or more other serum LPs, comprising (a) contacting the liquid

sample with a solid-support reagent contg. lectin attached to a solid support under conditions effective to bind LPa to the support bound lectin, (b) removing LPs in the sample which are not bound to the support and (c) assaying the LPa remaining after the removal.

Pref. the lectin binds specifically to LPa monosaccharide units selected from N-acetyl-D-glucosamine and N-acetylnuroaminic acid. The lectin may be e.g. wheat germ agglutinin, lima bean agglutinins, phytohaemagglutinin or horseshoe crab lectins. The assaying may include (i) treating the LPa with **cholesterol esterase** and a surfactant to release cholesterol from the LPa, (ii) reacting the released cholesterol with cholesterol oxidase to produce H<sub>2</sub>O<sub>2</sub> and (iii) assaying for produced H<sub>2</sub>O<sub>2</sub> using a peroxidase enzyme.

**USE/ADVANTAGE** - The assay method provides a direct LPa cholesterol determin. with a margin of error of + or - 1% for use in screening for coronary artery disease and advanced **atherosclerosis**.

3/3

Dwg.3/3

Dwg.3/3

L10 ANSWER 15 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1992-133595 [17] WPIDS  
 DNC C1992-062469  
 TI New tri cyclic heterocyclic derivs. are ACAT inhibitors - used for treating hypercholesterolaemia, **atherosclerosis**, myocardial infarction etc..  
 DC B02  
 IN IKEDA, H; MEGURO, K; TAWADA, H  
 PA (TAKE) TAKEDA CHEM IND LTD  
 CYC 17  
 PI EP 481243 A 19920422 (199217)\* EN 34p  
     R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE  
     CA 2052287 A 19920328 (199223)  
     JP 05009179 A 19930119 (199311) 21p  
     US 5264454 A 19931123 (199348) 19p  
     US 5418239 A 19950523 (199526) 18p  
 ADT EP 481243 A EP 1991-116099 19910921; CA 2052287 A CA 1991-2052287  
     19910926; JP 05009179 A JP 1991-202003 19910812; US 5264454 A US  
     1991-765182 19910925; US 5418239 A Div ex US 1991-765182 19910925, US  
     1993-117950 19930908  
 FDT US 5418239 A Div ex US 5264454  
 PRAI JP 1990-259657 19900927; JP 1991-202003 19910812  
 AB EP 481243 A UPAB: 19931006  
 Fused heterocycle derivs. of formula (I) and their salts are new. Ring A and ring B= opt. subst. benzene; X= N(O)m= C(R2), N(R3)-CO or O-CO; R2= H, alkyl or alkoxy; m= 0-1; R3= H or alkyl; Y= bond, NH, 1-2C alkylene or vinylene; R1= opt. subst. hydrocarbyl; n= 3-6. Ring A and ring B= benzene opt. subst. by 1-4 of halo, 1-6C alkyl (opt. subst. by halo), 1-6C alkoxy (opt. subst. by halo), 1-6C alkylthio (opt. subst. by halo), 1-3C acyloxy, di(1-6C alkyl); amino or OH (esp. A=benzene subst. by 1-3 of halo, 1-6C alkyl or OH and B= benzene). X= N= CR2, NR3CO, or OCO, R2= H or 1-6C alkoxy; R3= 1-6C alkyl; Y= NH or 1-2C alkylene; R1= 1-8C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl-(1-4C) alkyl, 6-10C aryl or 7-16C aralkyl all opt. subst. by 1-5 of halo, 1-6C alkyl (opt. subst. by halo), 1-6C alkoxy, (opt. subst. by halo), 1-6C alkylthio (opt. subst. by halo), 1-3C acyloxy, di(1-6C alkyl) amino or OH (esp. phenyl subst. by 1-3 of halo, 1-6C alkyl, 1-6C alkoxy, 1-6C acyloxy (sic), di(1-6C alkyl)amino or H (partic. 2,4-difluorophenyl)). n=3.  
 USE - (I) are acyl-CoA:cholesterol acyl transferase (ACAT) inhibitors ACAT inhibitors inhibit the absorption of dietary cholesterol from the intestinal tract, suppress the increase in cholesterol levels in the blood and suppress the accumulator of intracellular cholesterol. (I) are useful for treating hypercholesterolaemia and **atherosclerosis** and diseases associated with them e.g. ischaemic heart disease such as

myocardial infarction and cerebrovascular disorders such as cerebral infarction and cerebral apoplexy). (0/0)  
0/0

L10 ANSWER 16 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1991-361500 [49] WPIDS  
 DNC C1991-155829  
 TI Decreasing absorption of fats and cholesterol through intestinal wall - comprises admin. of carbamate ester which acts as pancreatic cholesterol esterase inhibitor.  
 DC B05  
 IN QUINN, D M  
 PA (UNIP) UNIV IOWA  
 CYC 1  
 PI US 5066674 A 19911119 (199149)\*  
 ADT US 5066674 A US 1990-533079 19900604  
 PRAI US 1990-533079 19900604  
 AB US 5066674 A UPAB: 19930928  
 The carbamate ester is of formula Z-X-C(=Y)NHR (I), Z = 2-naphthyl (opt. substd. by 1-8C alkyl, halogen, or 1-8C alkoxy) or p-acetamidophenyl. X and Y = O. R = 1-8C alkyl.  
 USE/ADVANTAGE - (I) act as pancreatic **cholesterol esterase** (CEase) inhibitors, for use as hypolipidaemic and hypocaloric agents. They pass through the GI tract unchanged, as they are poorly absorbed into the blood-stream and are resistant to CEase-catalysed hydrolysis. The method is useful in the treatment of obesity and **atherosclerosis**. Unit dosage of (I) is 0.01-1.0 mg/kg. administered orally.  
 In an example, cpds. (I) tested as inhibitors of the CEase-catalysed hydrolysis of p-nitrophenyl butyrate. The half-life of irreversible inhibition in the presence of 10 power -5 M inhibitor was 0.86 minutes for 2-naphthyl-n-octyl carbamate, 2.3 minutes for p-acetamidophenyl-n-hexyl carbamate and 29 minutes for p-acetamidophenyl n-butyl carbamate.  
 0/0

L10 ANSWER 17 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1991-150354 [21] WPIDS  
 DNC C1991-065001  
 TI 4-phenoxy phenyl carbamate ester derivs. - useful as **cholesterol ester hydrolase** inhibitors to treat coronary heart disease, **atherosclerosis**, etc..  
 DC B03 B05  
 IN COMMONS, T J; MEWSHAW, R E; STRIKE, D P; NEWSHAW, R E  
 PA (AMHP) AMERICAN HOME PROD CORP  
 CYC 10  
 PI EP 428385 A 19910522 (199121)\*  
 GB 2238542 A 19910605 (199123)  
 HU 55352 T 19910528 (199127)  
 CA 2029934 A 19910516 (199130)  
 FI 9005558 A 19910516 (199133)  
 PT 95869 A 19910913 (199140)  
 AU 9066534 A 19910718 (199141)  
 JP 03206071 A 19910909 (199142)  
 ZA 9009103 A 19920729 (199235) 71p  
 NZ 236061 A 19930225 (199312)  
 AU 635087 B 19930311 (199317)  
 HU 207842 B 19930628 (199332)  
 GB 2238542 B 19930901 (199335)  
 US 5391571 A 19950221 (199513) 16p  
 US 5512565 A 19960430 (199623) 12p  
 US 5602151 A 19970211 (199712) 11p  
 ADT EP 428385 A EP 1990-312382 19901113; GB 2238542 A GB 1990-24693 19901113;  
 JP 03206071 A JP 1990-311216 19901115; ZA 9009103 A ZA 1990-9103 19901113;

NZ 236061 A NZ 1990-236061 19901113; AU 635087 B AU 1990-66534 19901113;  
 HU 207842 B HU 1990-7132 19901115; GB 2238542 B GB 1990-24693 19901113; US  
 5391571 A CIP of US 1989-436841 19891115, Cont of US 1990-594241 19901009,  
 Cont of US 1991-771580 19911004, US 1993-62026 19930513; US 5512565 A CIP  
 of US 1989-436841 19891115, Cont of US 1990-594241 19901009, Cont of US  
 1991-771580 19911004, Div ex US 1993-62026 19930513, Div ex US 1994-277396  
 19940719, US 1995-413559 19950330; US 5602151 A CIP of US 1989-436841  
 19891115, Cont of US 1990-594241 19901009, Cont of US 1991-771580  
 19911004, Div ex US 1993-62026 19930513, Div ex US 1994-277396 19940719,  
 US 1995-572993 19951215

FDT AU 635087 B Previous Publ. AU 9066534; HU 207842 B Previous Publ. HU  
 55352; US 5512565 A Div ex US 5391571; US 5602151 A Div ex US 5391571

PRAI US 1990-594241 19901009; US 1989-436841 19891105; GB 1990-5537  
 19900312; US 1991-771580 19911004; US 1993-62026 19930513; US  
 1994-277396 19940719; US 1995-413559 19950330; US 1995-572993  
 19951215

AB EP 428385 A UPAB: 19930928  
 4-Phenoxyphenyl carbamate of formula (I) and their salts are new.  
 R1= opt. unsatd. 4-20C alkyl, 3-8C cycloalkyl, 1- or 2-adamantyl,  
 3-noradamantyl, 3-methyl-1-adamantyl, 1- or 9-fluorenyl, (3-8C  
 cycloalkyl)-(1-6C alkyl), phenyl or phenyl-(1-20C alkyl). R2= H or 1-6C  
 alkyl or R1 and R2 together form a heterocycle (i). X= -C(R7)(R8)-, NR9,  
 O or S. R7= H, 1-6C alkyl, OH, 2-6C alkanoyloxy, 1-6C hydroxyalkyl, CO2H,  
 2-16C alkoxycarbonyl or phenyl. R8= H or 1-6C alkyl or R7 and R8 together  
 are (CH2)m where m=2-6. R9= H, 1-6C alkyl, or phenyl, halo, NO2, or CN.  
 R10= H, 1-6C alkyl or 2-12C gem-dialkyl. n=0,1 or 2. R3, R4, R5, R6=  
 independently H, 1-6C alkyl, alkoxy, or perhaloalkyl halo, NO2, CN, CO2H  
 or 2-16C alkoxycarbonyl. When X= NR9 or R7= aminoalkyl, (I) can be present  
 in salt form.

USE/ADVANTAGE - As inhibitors of **cholesterol ester hydrolase**. (I) are therefore useful to treat coronary heart disease, . **atherosclerosis**, familial hypercholesterolaemia, hyperlipaemia, etc.

0/0

L10 ANSWER 18 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1990-348258 [46] WPIDS  
 CR 1991-178095 [24]; 1996-087083 [09]  
 DNC C1990-151144  
 TI Inhibition of intestinal cholesterol absorption - by oral admin of non-absorbable inhibitor of **cholesterol esterase**, esp.  
 high mol.wt. sulphated polysaccharide.

DC B04 D16  
 IN LANGE, L G; SPILBURG, C A  
 PA (LANG-I) LANGE L G; (SPIL-I) SPILBURG C A; (SCHI-I) SCHIERANO P  
 CYC 17  
 PI WO 9012579 A 19901101 (199046)\* 49p  
 RW: AT BE CH DE DK ES FR GB IT LU NL SE  
 W: AU CA JP US  
 AU 9055356 A 19901116 (199107)  
 US 5017565 A 19910521 (199123) 8p  
 US 5063210 A 19911105 (199147) 11p  
 EP 469079 A 19920205 (199206)  
 R: AT BE CH DE ES FR GB IT LI LU NL SE  
 JP 04503813 W 19920709 (199234) 19p  
 AU 633569 B 19930204 (199312)  
 EP 469079 B1 19941207 (199502) EN 29p  
 R: AT BE CH DE DK ES FR GB IT LI LU NL SE  
 DE 69014870 E 19950119 (199508)  
 ES 2064736 T3 19950201 (199511)  
 JP 08019001 B2 19960228 (199613) 19p  
 US 5616570 A 19970401 (199719)# 20p  
 CA 2053258 C 19980210 (199817)

US 5792832 A 19980811 (199839)  
 ADT US 5017565 A US 1989-340868 19890420; US 5063210 A US 1989-429398  
 19891031; EP 469079 A EP 1990-907923 19900420; JP 04503813 W JP  
 1990-506819 19900420, WO 1990-US2079 19900420; AU 633569 B AU 1990-55356  
 19900420; EP 469079 B1 EP 1990-907923 19900420, WO 1990-US2079 19900420;  
 DE 69014870 E DE 1990-614870 19900420, EP 1990-907923 19900420, WO  
 1990-US2079 19900420; ES 2064736 T3 EP 1990-907923 19900420; JP 08019001  
 B2 JP 1990-506819 19900420, WO 1990-US2079 19900420; US 5616570 A Cont of  
 WO 1990-US2079 19900420, Cont of US 1991-773875 19911018, US 1994-283723  
 19940801; CA 2053258 C CA 1990-2053258 19900420; US 5792832 A Cont of US  
 1989-429398 19891031, Cont of US 1989-434899 19891113, Cont of US  
 1992-856910 19920512, Div ex US 1994-350801 19941207, US 1995-461881  
 19950605

FDT JP 04503813 W Based on WO 9012579; AU 633569 B Previous Publ. AU 9055356,  
 Based on WO 9012579; EP 469079 B1 Based on WO 9012579; DE 69014870 E Based  
 on EP 469079, Based on WO 9012579; ES 2064736 T3 Based on EP 469079; JP  
 08019001 B2 Based on JP 04503813, Based on WO 9012579; US 5792832 A Cont  
 of US 5173408

PRAI US 1989-429398 19891031; US 1989-340868 19890420; US 1994-283723  
 19940801; US 1989-434899 19891113; US 1992-856910 19920512; US  
 1994-350801 19941207; US 1995-461881 19950605

AB WO 9012579 A UPAB: 19991221  
 Ingestible food prod. contains an effective amt. of a non-absorbable  
 synthetic **cholesterol esterase** inhibitor (I).  
 Inhibiting the intestinal absorption of cholesterol comprises admin. p.o.  
 a non-absorbable inhibitor of **cholesterol esterase** or  
 an antibody directed against **cholesterol esterase**.  
 Reducing serum cholesterol levels comprises admin. of a synthetic  
 non-absorbable sulphated polysaccharide in combination with an absorbed  
 cholesterol synthesis blocker, triglyceride lipase inhibitor or fatty acyl  
 cholesterol O-acyl transferase (ACAT) inhibitor.  
 USE/ADVANTAGE - (I), esp. sulphonated polysaccharides, decrease  
 intestinal absorption of cholesterol and fatty acid by inhibiting  
 pancreatic **cholesterol esterase**, which is a key enzyme  
 involved in dietary cholesterol absorption. (I) are stable and can be  
 incorporated in food prods., including baked prods. for dietary control of  
 serum cholesterol levels and **atherosclerosis** (I) are potent  
 inhibitors; are non-absorbable, so that side-effects are reduced; and are  
 inexpensive. Doses of cholesterol synthesis blockers or ACAT inhibitors  
 can be reduced, and side-effects minimized, by use with (I).  
 Dwg.0/10

L10 ANSWER 19 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1990-218740 [29] WPIDS  
 DNN N1990-169759 DNC C1990-094452  
 TI Determn. of net high density lipoprotein cholesterol content of serum - by  
 pptn. of other lipoprotein(s) then assaying cholesterol in lipase treated  
 and untreated samples, for assessing risk of vascular disease.  
 DC B04 D13 S03  
 IN MAINES, R Q  
 PA (MAIN-I) MAINES R Q  
 CYC 14  
 PI EP 378395 A 19900718 (199029)\*  
 R: AT BE CH DE ES FR GB LI LU NL SE  
 CA 2007645 A 19900713 (199039)  
 EP 378395 A3 19920701 (199333)  
 US 5453358 A 19950926 (199544) 5p  
 EP 378395 B1 19960814 (199637) EN 12p  
 R: AT BE CH DE DK ES FR GB LI LU NL SE  
 DE 69028023 E 19960919 (199643)  
 ADT EP 378395 A EP 1990-300287 19900110; EP 378395 A3 EP 1990-300287 19900110;  
 US 5453358 A Cont of US 1989-297080 19890113, US 1992-941669 19920908; EP  
 378395 B1 EP 1990-300287 19900110; DE 69028023 E DE 1990-628023 19900110,

EP 1990-300287 19900110  
 FDT DE 69028023 E Based on EP 378395  
 PRAI US 1989-297080 19890113; US 1992-941669 19920908  
 AB EP 378395 A UPAB: 19931119  
 Determin. of the net HDL cholesterol content of blood serum comprises (1) treating a sample with a pptg. agent which combines with LDL and VLDL particles in the serum; (2) centrifuging to remove ppt., leaving supernatant contg. HDL and free cholesterol (ch); (3) treating supernatant with enzyme which de-esterifies (ch), so as to break down HDL particles into (Ch) and fatty acid; (4) treating with (Ch) oxidase to oxidise all (Ch) to H<sub>2</sub>O<sub>2</sub> and cholest-4-en-3-one; (5) treating with peroxidase (POD); 4-amino-antipyrine (AAP) and chromogen to convert the H<sub>2</sub>O<sub>2</sub> produced to a quinone imine (QI); (6) measuring the absorbance of QI at a suitable wavelength; (7) repeating steps (3-6) on at least one (Ch)-contg. standard; (8) calculating the concn. of HDL and non-pptd. (Ch) from the equation (HDL + free (Ch) concn.) = S.C. x 2As/Ast. (As and Ast = absorbance of sample and standard respectively; S.C = concn. of the standard); (9) repeating steps (4-6) on separate samples of supernatant and standard, (10) calculating the non-pptd. free (Ch) concn. from the eqn. free (Ch) concn. = S.C. x 2As/Ast and (11) calculating net HDL cholesterol by subtraction of results from steps (8) and (10).

Also new is an emulsified diet supplement for increasing % HDL cholesterol in the blood consisting of a polyunsatd. lipid, phospholipid contg. essential fatty acids; a polysaccharide and an antioxidant.

USE - The measurement of HDL cholesterol is used to diagnose (and assess the risk of) vascular disease and **atherosclerosis**. The new diet supplement reduces the risk of such diseases. @ (9pp Dwg.No.0/0)  
0/0

L10 ANSWER 20 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1989-357528 [49] WPIDS  
 DNN N1989-271750 DNC C1989-158494  
 TI Determn. of cholesterol-contg. lipo protein fractions - by electrophoresis on a thin-layer carrier matrix.  
 DC B04 D16 S03 S05  
 IN AUFENANGER, J  
 PA (AUFENANGER J; (IMMO) IMMUNO CHEM MEDIZINISCHE PROD; (IMMO) IMMUNO AG; (IMMO) IMMUNO CHEM MEDIZINISCHE PROD AG  
 CYC 11  
 PI DE 3817747 A 19891130 (198949)\* 6p  
 EP 344580 A 19891206 (198949) DE  
 R: AT BE CH DE FR GB IT LI NL SE  
 EP 344580 B1 19941228 (199505) DE 9p  
 R: AT BE CH DE FR GB IT LI NL SE  
 DE 58908816 G 19950209 (199511)  
 US 5385828 A 19950131 (199511)# 6p  
 ADT DE 3817747 A DE 1988-3817747 19880525; EP 344580 A EP 1989-109261 19890523; EP 344580 B1 EP 1989-109261 19890523; DE 58908816 G DE 1989-508816 19890523, EP 1989-109261 19890523; US 5385828 A Cont of US 1989-359800 19890601, US 1992-981992 19921124  
 FDT DE 58908816 G Based on EP 344580  
 PRAI DE 1988-3817747 19880525  
 AB DE 3817747 A UPAB: 19930923  
 (A) In a new procedure for the determination of the relative amounts of all cholesterol-contg. lipoproteins in body fluids in which the lipoproteins of an aliquot of body fluid are separated electrophoretically on a carrier matrix and subsequently detected by means of an enzymatic reaction comprising incubation of the carrier matrix with cholesterolase and cholesterol dehydrogenase, leading to the formation of a detectable complex, and the relative amounts of the different lipoprotein classes are determined, the electrophoresis is carried out on a thin-layer matrix. (B) In a new procedure for the determination of the concentration of all cholesterol-contg. lipoproteins in body fluids, the

relative amounts determined by the above procedure are expressed in proportion to the total cholesterol concentration of the body fluid.

**USE/ADVANTAGE** - Determination of low- and high-density lipoprotein cholesterol as an aid to the diagnosis of susceptibility to **atherosclerosis** and cardiac infarction. The procedure is rapid, reliable and reproducible, and gives results in archivable form.

L10 ANSWER 21 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1989-292337 [40] WPIDS  
 DNC C1989-129545  
 TI Inhibition of intestinal cholesterol and fatty acid absorption - by admin. of heparin, its sub-fraction or heparinase.  
 DC B04 D16  
 IN KINNUNEN, P M; LANGE, L G; SPILBURG, C A  
 PA (LANG-I) LANGE L G; (CVTH-N) CV THERAPEUTICS; (JEWI-N) JEWISH HOSPITAL ST  
 CYC 13  
 PI WO 8908456 A 19890921 (198940)\* 35p  
 RW: AT BE CH DE FR GB IT LU NL SE  
 W: AU JP  
 AU 8934348 A 19891005 (199001)  
 US 5352601 A 19941004 (199439) 14p  
 US 5429937 A 19950704 (199532) 13p  
 US 5492822 A 19960220 (199613) 12p  
 ADT WO 8908456 A WO 1989-US787 19890227; US 5352601 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, US 1992-936103 19920826; US 5429937 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, Div ex US 1992-936103 19920826, US 1994-311862 19940926; US 5492822 A CIP of US 1988-168424 19880315, Cont of US 1989-312255 19890222, Cont of US 1990-544212 19900626, Cont of US 1991-655289 19910214, Div ex US 1992-936103 19920826, Div ex US 1994-311862 19940926, US 1995-386433 19950210  
 FDT US 5429937 A Div ex US 5352601; US 5492822 A Div ex US 5352601, Div ex US 5429937  
 PRAI US 1989-312255 19890222; US 1988-168424 19880315; US 1990-544212 19900626; US 1991-655289 19910214; US 1992-936103 19920826; US 1994-311862 19940926; US 1995-386433 19950210  
 AB WO 8908456 A UPAB: 19930923  
 Inhibiting intestinal cell endogenous heparin mediated absorption of cholesterol or fatty acids in mammals comprises orally administering heparin, an active heparin subfraction or heparinase.  
 USE - Heparin can compete for binding to **cholesterol esterase**, displacing the enzyme from the membrane of the intestinal cell and greatly diminishing the intestinal absorption of cholesterol and cholesterol derived fatty acids. Also exogenous heparin displaces the pancreatic enzymes, such as triglyceride lipase which hydrolyse triglycerides into free fatty acids, from the membrane of the intestinal cell.

6

L10 ANSWER 22 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1988-285789 [41] WPIDS  
 DNN N1988-217232 DNC C1988-126927  
 TI New sterol polyene derivs. - useful as fluorescent membrane probes.  
 DC B01 B04 S03  
 IN DREW, J; PROULX, P R; SZABO, A G  
 PA (CANA) CANADIAN PATENTS & DEV LTD; (MORA-I) MORAND P; (CANA) NAT RES COUNCIL CANADA; (UYOT-N) UNIV OTTAWA  
 CYC 2  
 PI CA 1241947 A 19880913 (198841)\* 27p  
 US 4879069 A 19891107 (199003) 10p  
 US 4980280 A 19901225 (199103)

ADT CA 1241947 A CA 1985-482887 19850531; US 4879069 A US 1986-867565  
 19860528; US 4980280 A US 1989-359368 19890531

PRAI CA 1985-482887 19850531

AB CA 1241947 A UPAB: 19930923

Olefinic sterol derivs. of formula (I) are new, where R=H or an acyl gp.  
 suitable for use in **cholesterol esterase** assays; A=a  
 polyene gp. of formula A1-A4, R1=H, 1-4C alkyl, 2-4C alkenyl, 2-4C alkynyl  
 or aryl; R2=(CH=CH)nQ; n=0-3; Q=CH=CH<sub>2</sub>, phenyl, naphthyl, tricyclic aryl,  
 tetracyclic aryl or a sterol gp. of formula Q1.

USE - (I) are useful as fluorescent probes for investigating the  
 behaviour of cholesterol in vivo, for investigating the properties and  
 cholesterol content of cell membranes, and for investigation and early  
 diagnosis of **atherosclerosis**.

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L10 ANSWER 23 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1988-269131 [38] WPIDS

DNN N1988-204158 DNC C1988-120103

TI Lipid analysis in blood serum or plasma - involves liq. chromatography and  
 preliminary enzymatic hydrolysis of stabilising proteins, to increase  
 accuracy.

DC B04 D16 S03

IN DVORKIN, V I; VAVKUSHEVS, I N; ZOLOTOV, N N

PA (AMCA-R) A MED CARDIOL CENTR

CYC 1

PI SU 1377733 A 19880229 (198838)\* 3p

ADT SU 1377733 A SU 1985-3922509 19850704

PRAI SU 1985-3922509 19850704

AB SU 1377733 A UPAB: 19930923

To determine glycerides treatment (of the sample) involves phospholipase.

To determine ethers (

) of cholesterol and steroids treatment involves lipase. To determine  
 phospholipides treatment involves **cholesterol-esterase**

. As previously, the method involves:- extg. lipids by an organic solvent;  
 liq. chromatography.

USE/ADVANTAGE - Increased accuracy in the analysis of lipids in blood  
 serum or plasma in biochemistry and medical practice, esp. in  
 investigation of lipid exchange and pathogenesis of  
**atherosclerosis**. Typically, in analysis of cholesterol ethers the  
 proposed method reduces the error from 100+% to 4-6%. In analysis of  
 acyglycerol the proposed method reduces error from 10-12% to 5-6%.

Bul.8/29.2.88.

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L10 ANSWER 24 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 1988-121051 [18] WPIDS

DNN N1988-091887 DNC C1988-054205

TI Specific measurement of high density lipoprotein cholesterol in serum - by  
 incubation with esterase and oxidase, and kinetic monitoring of hydrogen  
 peroxide formation.

DC A96 B04 D16 S03

IN KERSCHER, L; PAUTZ, B; TRUNK, G; ZIEGENHORN, J

PA (BOEFL) BOEHRINGER MANNHEIM GMBH; (BOEFL) OEHRLINGER MANNHEIM GMBH

CYC 20

PI EP 265933 A 19880504 (198818)\* DE 16p

R: AT BE CH DE ES FR GB GR IT LI LU NL SE

DE 3636851 A 19880511 (198820)

AU 8780446 A 19880505 (198826)

JP 63126498 A 19880530 (198827)

FI 8704749 A 19880430 (198831)

US 4892815 A 19900109 (199010) 11p

CA 1309645 C 19921103 (199250)

EP 265933 B1 19930203 (199305) DE 19p

R: AT BE CH DE ES FR GB GR IT LI LU NL SE  
DE 3784004 G 19930318 (199312)  
FI 90882 B 19931231 (199404)  
JP 07034760 B2 19950419 (199520) 10p  
ADT EP 265933 A EP 1987-115841 19871028; DE 3636851 A DE 1986-3636851  
19861029; JP 63126498 A JP 1987-269522 19871027; US 4892815 A US  
1987-107467 19871006; CA 1309645 C CA 1987-549035 19871009; EP 265933 B1  
EP 1987-115841 19871028; DE 3784004 G DE 1987-3784004 19871028, EP  
1987-115841 19871028; FI 90882 B FI 1987-4749 19871028; JP 07034760 B2 JP  
1987-269522 19871027  
FDT DE 3784004 G Based on EP 265933; FI 90882 B Previous Publ. FI 8704749; JP  
07034760 B2 Based on JP 63126498  
PRAI DE 1986-3636851 19861029  
AB EP 265933 A UPAB: 19950530  
Specific determination of HDL-cholesterol in presence of the LDL fraction  
of serum lipoproteins comprises treating with **cholesterol**  
**esterase** (CE) to release cholesterol which is oxidised with  
cholesterol oxidase (CO) and O<sub>2</sub> to form H<sub>2</sub>O<sub>2</sub>, then kinetic measurement of  
H<sub>2</sub>O<sub>2</sub> formation or of O<sub>2</sub> consumption.  
The new feature is that measurement is carried out at 2-15 min after  
start of oxidase reaction at 20-40 deg C for a predetermined time  
interval. During measurement concns maintained in the reaction soln are:  
CE 0.05-30 u/ml; Co 0.1-50 U/ml; bile acid surfactant 1-20 mM and nonionic  
surfactant 0.1-10 g/l, while pH is 5-9. Also new is a reagent which  
provides the specified concns. of CO, CE and surfactants, plus pH 5-9  
buffer and a system for photometric measurement of H<sub>2</sub>O<sub>2</sub>.  
ADVANTAGE - The HDL component is measured with a simple reagent in a  
single step, and the same sample can also be used to provide a measure of  
total cholesterol.  
0/5  
Dwg.0/5

L10 ANSWER 25 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
AN 1987-087376 [13] WPIDS  
DNN N1987-065510 DNC C1987-036259  
TI HDL cholesterol specific determination in serum or plasma - by incubation  
with cholesterol oxidase and a nonionic detergent.  
DC A96 B04 D16 S03  
IN KERSCHER, L; PAUTZ, B; SIEDEL, J; ZIEGENHORN, J  
PA (BOEFL) BOEHRINGER MANNHEIM GMBH  
CYC 19  
PI DE 3533288 A 19870326 (198713)\* 8p  
EP 218127 A 19870415 (198715) DE 11p  
R: AT BE CH DE FR GB IT LI LU NL SE  
AU 8661163 A 19870319 (198718)  
JP 62069999 A 19870331 (198718)  
FI 8603752 A 19870319 (198727)  
DK 8604459 A 19870319 (198731)  
ES 2001417 A 19880516 (198921)  
US 4851335 A 19890725 (198937) 7p  
EP 218127 B 19891213 (198950) DE  
R: AT BE CH DE FR GB IT LI LU NL SE  
DE 3667492 G 19900118 (199004)  
KR 8903948 B 19891013 (199040)  
JP 06016720 B2 19940309 (199413)  
ADT DE 3533288 A DE 1985-3533288 19850918; EP 218127 A EP 1986-112875  
19860910; JP 62069999 A JP 1986-218274 19860918; ES 2001417 A ES 1986-1650  
19860905; US 4851335 A US 1986-908031 19860916; EP 218127 B EP 1986-112875  
19860918; JP 06016720 B2 JP 1986-218274 19860918  
FDT JP 06016720 B2 Based on JP 62069999  
PRAI DE 1985-3533288 19850918  
AB DE 3533288 A UPAB: 19930922  
A specific determination of HDL-cholesterol in serum or plasma by

incubation with a cholesterol detection system contg. cholesterol oxidase and **cholesterol esterase** in buffered aq. medium and measurement of a prod. of the cholesterol oxidase reaction or oxygen consumption comprises (1) an incubation carried out in the presence of a bile acid or bile acid deriv. salt or of dioctyl sulphosuccinate, (2) carrying out a first measurement, (3) a non-ionic detergent contg. polyethylene oxide gps. or a sec. alkanesulphonate is added and the mixt. is again incubated, (4) a second measurement is carried out, and (5) the HDL-cholesterol amt. is determined from the difference between the first and second measurements.

New reagent of the new specific determination contains amts. w.r.t. ready-to-use aq. soln. 0.1-10 U/ml **cholesterol esterase**, 0.005-10 U/ml cholesterol oxidase, 20-500 mmol/l buffer substance pH 6.0-8.0, 0.2-20 mmol/l bile acid or bile acid deriv. salt or dioctyl-sulphosuccinate and, separately, 0.02-2% non-ionic detergent contg. polyethylene oxide gps. or sec. alkanesulphonate and, opt. 0.05-2% 1-3C alcohol.

USE/ADVANTAGE - Determination of the fraction of cholesterol bound in HDL- in the diagnosis of **atherosclerosis** or of the risk of cardiac infarct. HDL-cholesterol can be determined directly without previous sepn. of LDL-cholesterol esters, VLDL-cholesterol esters, VLDL-cholesterol and chylomicron-cholesterol from the specimen.

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L10 ANSWER 26 OF 26 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD  
 AN 1983-766269 [38] WPIDS  
 DNC C1983-089829  
 TI Low density lipoprotein fraction cholesterol specific determn. - in presence of high-density lipoprotein fraction using **cholesterol esterase** and **cholesterol oxidase** in the presence of surfactant.  
 DC B04 D16 J04  
 IN BARTL, K; RODER, A; WEHMEYER, G; ZIEGENHORN, J  
 PA (BOEFL) BOEHRINGER MANNHEIM GMBH  
 CYC 13  
 PI EP 88420 A 19830914 (198338)\* DE 21p  
     R: AT BE CH DE FR GB IT LI LU NL SE  
     DE 3208253 A 19830915 (198338)  
     JP 58165800 A 19830930 (198345)  
     US 4544630 A 19851001 (198542)  
     EP 88420 B 19860924 (198639) DE  
       R: AT BE CH DE FR GB IT LI LU NL SE  
       DE 3366371 G 19861030 (198645)  
 ADT EP 88420 A EP 1983-102231 19830307; US 4544630 A US 1983-468792 19830222  
 PRAI DE 1982-3208253 19820308  
 AB EP 88420 A UPAB: 19930925  
 New procedure is claimed for the specific determination of LDL-fraction cholesterol in the presence of the serum lipoprotein HDL fraction involving the use of **cholesterol esterase** to release the cholesterol, oxidation of the released cholesterol with cholesterol oxidase and oxygen to form H<sub>2</sub>O<sub>2</sub> and cholestenone, and kinetic measurement of the change in one of the components of the oxidase reaction (esp. H<sub>2</sub>O<sub>2</sub> formation). In this procedure, the measurement is carried out in a predetermined time interval, and the reaction soln. is adjusted to a surfactant concn. of 0.01-1.5 mmol/l, a **cholesterol esterase** concn. of 0.1-30U/ml, and a pH of 6.5-8.0.  
 New reagent for carrying out the above procedure contains 200-1000 U/l cholesterol oxidase, 1000-3000 U/l peroxidase, 2000-10000 U/l **cholesterol esterase**, 0.10-0.16 mmol/l surfactant, 2-20 mmol/l phenol, 0.5-3 mmol/l 4-aminoantipyrine, and 70-130 mmol/l tris/HCl pH 7.3-7.7.  
 Determination of LDL (low density lipoprotein) fraction cholesterol for the differential diagnosis of lipid metabolism disorders, e.g.

Ozga 09/775,517

hyparcholesterolemia of hypertriglyceridaemia leading to  
**atherosclerosis** and cardia infarct.

The new procedure permits direct enzymatic determination of LDL cholesterol without precipitation reactions or fraction separations. It is based on the finding that under specified surfactant concn., enzyme concn. and pH conditions enzymatic hydrolysis of the LDL-cholesterol is substantially faster than that of HDL-cholesterol.

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Ozga 09/775,517

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FILE 'BIOSIS' ENTERED AT 12:17:06 ON 18 OCT 2001

FILE 'REGISTRY' ENTERED AT 12:17:09 ON 18 OCT 2001  
E LYSOSOMAL ACID LIPASE/CN

L1 1 S E3

FILE 'BIOSIS' ENTERED AT 12:17:25 ON 18 OCT 2001

L2 776 S L1  
L3 1315 S ESTERASE (2A) CHOLESTEROL? OR CHOLESTERASE# OR CHOLESTERIN ES  
L4 231 S LYSOSOMAL ACID LIPASE# OR STEROL (W) (ESTER HYDROLASE# OR EST  
L5 1531 S L2-L4  
L6 49186 S ATHEROSCLER? OR ANTIARTERIOSCLER? OR ANTIATHEROSCLER?  
L7 142 S L5 AND L6  
L8 17840 S MANNOSE OR ACETYL GLYCOSYLAT? OR ACETYLGLYCOSYLAT?  
L9 17841 S MANNOSE OR ACETYL GLYCOSYLAT? OR ACETYLGLYCOSYLAT?  
L10 110369 S VECTOR#  
L11 326 S WOLMAN? OR CHOLESTER? ESTER STORAGE DISEAS?  
L12 0 S L7 AND L9  
L13 0 S L7 AND L10  
L14 14 S L7 AND L11  
L15 5 S LIPID HYDROLYZ? (2A) (PROTEIN# OR POLYPEPTIDE# OR ENZYME?)  
L16 0 S L15 AND L6  
L17 0 S PLASMID? AND L7  
L18 17373 S LYSOSOME?  
L19 13 S L18 AND L7  
L20 326 S RECEPTOR# (5A) L18  
L21 0 S L20 AND L7  
L22 205801 S MUTAT?  
L23 7 S L7 AND L22  
L24 15-S L14 OR L23

FILE 'BIOSIS' ENTERED AT 12:27:16 ON 18 OCT 2001

=> d bib ab it 1-15

L24 ANSWER 1 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS  
AN 2000:159815 BIOSIS  
DN PREV200000159815  
TI Subclinical course of **cholesteryl ester**  
**storage disease** in an adult with hypercholesterolemia,  
accelerated atherosclerosis, and liver cancer.  
AU Elleder, Milan (1); Chlumska, Alena; Hynek, Josef; Poupetova, Helena;  
Ledvinova, Jana; Maas, Sylke; Lohse, Peter

CS (1) Institute of Inherited Metabolic Disorders, 1st Faculty of Medicine and General Faculty Hospital, Charles University Prague, Ke Karlovu 2, 128 00, Praha, 2 Czech Republic

SO Journal of Hepatology., (March, 2000) Vol. 32, No. 3, pp. 528-534.  
ISSN: 0168-8278.

DT Article

LA English

SL English

AB Few cases of asymptomatic **cholesteryl ester storage disease** (CESD) due to low enzymatic activity of **human lysosomal acid lipase/cholesteryl ester hydrolase** (hLAL) have been reported thus far in adults. Here, we describe a 51-year-old man with a long clinical history of mixed hyperlipoproteinemia and severe premature **atherosclerosis**, but with no signs of hepatomegaly, liver dysfunction, or splenomegaly. The disease was discovered by chance in a biopsy performed because of suspected liver cancer (proven to be a cholangiocarcinoma). Residual hLAL activity in peripheral leukocytes was determined to be 6% of control values. DNA sequence and restriction fragment length polymorphism analysis demonstrated that the patient was a compound heterozygote for the prevalent CESD exon 8 splice site **mutation** (G934A) and the deletion of a C (nucleotide 673, 674, or 675) in exon 6 of the hLAL gene, resulting in premature termination of protein translation at residue 195. The patient died of liver failure as a consequence of extensive tumor infiltration at age 52. Lipid analysis revealed moderate cholesteryl ester storage in the liver and in the suprarenal cortex, and massive accumulation in the testicular histiocytes and Leydig cells, resulting in a pronounced secondary atrophy of the seminiferous tubules. Our case study demonstrates that hepatomegaly is an inconstant feature, even in CESD patients compound heterozygous for a **Wolman mutation** which results in complete loss of hLAL enzymic activity. It also highlights the need to be aware of this condition as it may be underdiagnosed.

IT Major Concepts

Cardiovascular Medicine (Human Medicine, Medical Sciences); Gastroenterology (Human Medicine, Medical Sciences); Oncology (Human Medicine, Medical Sciences); Metabolism

IT Diseases

**atherosclerosis**: vascular disease; **cholesteryl ester storage disease**: clinical pathology, diagnosis, genetic disease, histopathology, metabolic disease; **hypercholesterolemia**: metabolic disease; **liver cancer**: digestive system disease, neoplastic disease; **liver failure**: digestive system disease

IT Chemicals & Biochemicals

**human lysosomal acid lipase/cholesteryl ester hydrolase**: activity; **human hLAL gene [human lysosomal acid lipase/cholesteryl ester hydrolase gene]** (Hominidae): **mutation**

IT Alternate Indexing

**Atherosclerosis** (MeSH); **Hypercholesterolemia** (MeSH); **Liver Neoplasms** (MeSH); **Liver Failure** (MeSH)

IT Methods & Equipment

DNA sequencing: genetic method; HPTLC chromatography: analytical method; electron microscopy: microscopy method; liver biopsy: diagnostic method; restriction fragment length polymorphism analysis: genetic method

IT Miscellaneous Descriptors

Case Study

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae): male, middle age, patient

## ORGN Organism Superterms

Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L24 ANSWER 2 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS  
 AN 1999:516512 BIOSIS  
 DN PREV199900516512  
 TI Hepatosplenomegalic lipidosis: What unless Gaucher? Adult  
**cholesteryl ester storage disease**  
 (CESD) with anemia, mesenteric lipodystrophy, increased plasma  
 chitotriosidase activity and a homozygous **lysosomal acid**  
**lipase -1 exon 8 splice junction mutation.**  
 AU vom Dahl, Stephan (1); Harzer, Klaus; Rolfs, Arndt; Albrecht, Bettina;  
 Niederau, Claus; Vogt, Christoph; van Weely, Sonja; Aerts, Johannes;  
 Mueller, Gerd; Haeussinger, Dieter  
 CS (1) Division of Gastroenterology, Heinrich-Heine-University, Moorenstrasse  
 5, D-40 225, Duesseldorf Germany  
 SO Journal of Hepatology, (Oct., 1999) Vol. 31, No. 4, pp. 741-746.  
 ISSN: 0168-8278.  
 DT Article  
 LA English  
 SL English  
 AB A 36-year-old woman was admitted for hepatosplenomegaly and anemia. Bone  
 marrow cytology showed "sea-blue histiocytes", vacuolated macrophages and  
 plasma cells. As primary liver disease, malignancy or hematologic  
 disorders were excluded, and plasma chitotriosidase activity was increased  
 27-fold over control, the presence of a lysosomal storage disease was  
 suspected. Biochemical analysis of skin fibroblasts revealed normal  
 glucocerebrosidase and sphingomyelinase activity, but lipid analysis  
 showed a more than 15-fold accumulation of cholesterol esters within the  
 cells. The activity of **lysosomal acid lipase**  
 (LAL) in fibroblast homogenates was decreased to 12% of control subjects.  
**Mutational analysis** of the patient's blood showed the homozygous  
**GfwdarwA mutation** at position -1 of the exon 8 splice donor site  
 (E8SJM-allele) known for adult **cholesteryl ester**  
**storage disease** (CESD); the polymorphic background was  
 that of the complex haplotype -6Thr, 2Gly, 894 GfwdarwA. Based on  
 clinical, laboratory, cytological and biochemical findings, CESD can  
 clearly be separated from other more frequent inherited lysosomal storage  
 diseases, e.g. atypical forms of Gaucher disease.  
 IT Major Concepts  
     Gastroenterology (Human Medicine, Medical Sciences); Medical Genetics  
     (Allied Medical Sciences); Metabolism  
 IT Diseases  
     anemia: blood and lymphatic disease; **atherosclerosis:**  
     vascular disease; chitotriosidase: activity; **cholesteryl**  
**ester storage disease:** genetic disease,  
     metabolic disease; hepatosplenomegaly: blood and lymphatic disease,  
     digestive system disease; hypercholesterolemia: metabolic disease;  
     mesenteric lipodystrophy: congenital disease, genetic disease,  
     metabolic disease, digestive system disease; sea-blue histiocytes:  
     blood and lymphatic disease, genetic disease, metabolic disease;  
     Gaucher disease: behavioral and mental disorders, genetic disease,  
     metabolic disease, blood and lymphatic disease; Niemann-Pick disease:  
     behavioral and mental disorders, blood and lymphatic disease, genetic  
     disease, metabolic disease, nervous system disease  
 IT Chemicals & Biochemicals  
     **lysosomal acid lipase:** activity; human  
     **lysosomal acid lipase gene** (Hominidae):  
     exon 8, homozygous splice junction **mutation**  
 IT Alternate Indexing  
     Anemia (MeSH); **Atherosclerosis** (MeSH); Gaucher's Disease  
     (MeSH); Hypercholesterolemia (MeSH); Niemann-Pick Disease (MeSH)  
 IT Miscellaneous Descriptors

## Case Study

ORGN Super Taxa  
Hominidae: Primates, Mammalia, Vertebrata, Chordata, AnimaliaORGN Organism Name  
human (Hominidae): adult, female, patientORGN Organism Superterms  
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 9026-00-0 (LYSOSOMAL ACID LIPASE)

L24 ANSWER 3 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1999:441210 BIOSIS

DN PREV199900441210

TI Splice-site **mutations** in **atherosclerosis** candidate genes: Relating individual information to phenotype.

AU von Kodolitsch, Yskert; Pyeritz, Reed E.; Rogan, Peter K. (1)

CS (1) Section of Molecular Genetics and Molecular Medicine, Children's Mercy Hospital and Clinics, 2401 Gillham Road, Kansas City, MO, 64108 USA

SO Circulation, (Aug. 17, 1999) Vol. 100, No. 7, pp. 693-699.  
ISSN: 0009-7322.

DT Article

LA English

SL English

AB Background-Nucleotide variants in several genes for lipid and methionine metabolism influence the risk of premature **atherosclerosis**. Ten percent of single nucleotide substitutions in these genes involve mRNA splice sites. The effects of some of these changes on splicing and on phenotypic severity are not inherently obvious. Methods and Results-Using an information theory-based model, we measured the individual information content ( $R_i$ , in bits) of splice sites adjacent to 289 **mutations** (including 31 splice-site **mutations**) in the **atherosclerosis** candidate genes APOAII, APOB, APOCII, APOE, CBS, CETP, LCAT, LIPA, LDLR, and LPL. The predictions of information analysis were then corroborated by published mRNA analyses. The  $R_i$  values of mutant sites were consistent with either complete ( $n=17$ ) or partial ( $n=8$ ) inactivation of these sites. Seven **mutations** were predicted to activate cryptic splice sites. Predicted inactive mutant sites were associated with either "average" or "severe" dyslipidemia and commensurate reductions in protein levels or activity, whereas **mutations** expected to exhibit residual splicing had average or "mild" effects on lipid and protein expression. Conclusions-Information analysis of splice-junction variants in **atherosclerosis** candidate genes distinguishes inactive from leaky splice sites and identifies activated cryptic sites. Predicted changes in splicing were related to phenotypic severity.

IT Major Concepts

Cardiovascular System (Transport and Circulation); Molecular Genetics (Biochemistry and Molecular Biophysics)

IT Diseases

**atherosclerosis**: phenotypic severity, vascular disease

IT Chemicals &amp; Biochemicals

human APOAII gene [human apolipoprotein-AII gene] (Hominidae):

**atherosclerosis** candidate gene, splice-site **mutation**;

human APOB gene [human apolipoprotein-B gene] (Hominidae):

**atherosclerosis** candidate gene, splice-site **mutation**;

human APOCII gene [human apolipoprotein-CII gene] (Hominidae):

**atherosclerosis** candidate gene, splice-site **mutation**;

human APOE gene [human apolipoprotein-E gene] (Hominidae):

**atherosclerosis** candidate gene, splice-site **mutation**;

human CBS gene [human cystathione beta-synthase gene] (Hominidae):

**atherosclerosis** candidate gene, splice-site **mutation**;

human CETP gene [human cholesterlyl ester transfer protein gene]

(Hominidae): **atherosclerosis** candidate gene, splice-site **mutation**;

human LCAT gene [human lecithin cholesterol

transferase gene] (Hominidae): **atherosclerosis** candidate gene, splice-site **mutation**; human LDLR gene [human low density lipoprotein receptor gene] (Hominidae): **atherosclerosis** candidate gene, splice-site **mutation**; human LIPA gene [human **lysosomal acid lipase A** gene] (Hominidae): **atherosclerosis** candidate gene, splice-site **mutation**; human LPL gene [human lipoprotein lipase gene] (Hominidae): **atherosclerosis** candidate gene, splice-site **mutation**

IT Alternate Indexing

**Atherosclerosis** (MeSH)

IT Miscellaneous Descriptors

mRNA splicing [messenger RNA splicing]: information theory-based model, **mutational severity**

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae)

ORGN Organism Supertaxa

Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 20910-06-9D (CHOLESTERYL)

9001-62-1 (LIPASE)

9004-02-8 (LIPOPROTEIN LIPASE)

L24 ANSWER 4 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1998:95468 BIOSIS

DN PREV199800095468

TI Clinical, biochemical and histological analysis of seven patients with **cholesteryl ester storage disease**.

AU Tylki-Szymanska, Anna (1); Rujner, Jolanta; Lugowska, Agnieszka; Sawnor-Korszynska, Danuta; Wozniewicz, Bogdan; Czarnowska, Elzbieta

CS (1) Dep. Metab. Dis., Child. Memorial Health Inst., Al. Dzieci Polskich 20, 04-736 Warsaw Poland

SO Acta Paediatrica Japonica, (Dec., 1997) Vol. 39, No. 6, pp. 643-646. ISSN: 0374-5600.

DT Article

LA English

AB **Lysosomal acid lipase (LAL)** deficiency leads to two phenotypically different diseases: **cholesteryl ester storage disease** (CESD) and **Wolman's disease**. **Lysosomal acid lipase** hydrolyzes cholesteryl esters and triglycerides. Deficiency of LAL results in intralysosomal storage of cholesteryl esters and triglycerides. CESD has a chronic and benign course and is characterized by hepatomegaly and mild hypercholesterolemia. It leads to fibrosis (cirrhosis) and early **atherosclerosis**. This report presents the clinical, biochemical and microscopic data of seven patients with CESD followed up over 10 years. The physical development of all the study children remained within the normal range; 7 patients had hepatomegaly and 6 also had splenomegaly. Three patients had normal cholesterol, triglycerides and transaminases values; the other four had slightly elevated levels for these parameters. The activity of LAL in all patients was reduced to below 30% of the lower normal value. Histologically, cholesteryl crystals and lipid storage vacuoles in Kupffer cells were present in all examined patients except one. Accumulation of cholesteryl esters was visible on thin-layer chromatography of lipid extracts obtained from liver biopsies.

IT Major Concepts

Metabolism

IT Diseases

**cholesteryl ester storage disease**

: metabolic disease

IT Chemicals & Biochemicals

cholesterol; cholesteryl esters; lysosomal acid

lipase; transaminases; triglycerides  
IT Miscellaneous Descriptors  
biochemical analysis; clinical analysis; histological analysis  
ORGN Super Taxa  
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia  
ORGN Organism Name  
human (Hominidae): child  
ORGN Organism Supertterms  
Animals; Chordates; Humans; Mammals; Primates; Vertebrates  
RN 20910-06-9D (CHOLESTERYL)  
57-88-5 (CHOLESTEROL)  
9031-66-7D (TRANSAMINASES)

L24 ANSWER 5 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS  
AN 1997:96028 BIOSIS  
DN PREV199799395231  
TI Importance of defined **mutations** in the LAL gene for the manifestation of CESD and WD and characterization of the LAL promoter.  
AU Aslanidis, C.; Ries, S.; Buechler, C.; Fehringer, P.; Schmitz, G.  
CS Inst. Clin. Chem. Lab. Med., Univ. Regensburg, 93042 Regensburg Germany  
SO Molecular Biology of the Cell, (1996) Vol. 7, No. SUPPL., pp. 296A.  
Meeting Info.: Annual Meeting of the 6th International Congress on Cell Biology and the 36th American Society for Cell Biology San Francisco, California, USA December 7-11, 1996  
ISSN: 1059-1524.  
DT Conference; Abstract; Conference  
LA English  
IT Major Concepts  
Biochemistry and Molecular Biophysics; Cardiovascular Medicine (Human Medicine, Medical Sciences); Cardiovascular System (Transport and Circulation); Cell Biology; Dermatology (Human Medicine, Medical Sciences); Development; Enzymology (Biochemistry and Molecular Biophysics); Genetics; Integumentary System (Chemical Coordination and Homeostasis); Metabolism; Molecular Genetics (Biochemistry and Molecular Biophysics)  
IT Chemicals & Biochemicals  
LIPASE; CHOLESTERYL  
IT Miscellaneous Descriptors  
ACCUMULATION; ANALYTICAL METHOD; AP2; AUTOSOMAL RECESSIVE DISORDER; CELL BIOLOGY; CELL CULTURE; CESD; CHOLESTERYL ESTER  
**STORAGE DISEASE**; CHOLESTERYL ESTERS; ENZYMOLOGY; EXPRESSION; GENE STRUCTURE; GENETIC DISEASE; LAL GENE; LAL GENE mRNA; LAL PROMOTER; **LYSOSOMAL ACID LIPASE** GENE; LYSOSOMAL ACID LIPASE MESSENGER RNA; LYSOSOMAL ACID LIPASE mRNA; LYSOSOMAL ACID LIPASE PROMOTER; METABOLIC DISEASE; MOLECULAR GENETICS; **MUTATIONS**; PATIENT; PREMATURE **ATHEROSCLEROSIS**; SP1; TRANSCRIPTION FACTOR; TRANSCRIPTION START SITE; TRIGLYCERIDES; VASCULAR DISEASE; WD; **WOLMAN** DISEASE  
ORGN Super Taxa  
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia  
ORGN Organism Name  
human (Hominidae)  
ORGN Organism Supertterms  
animals; chordates; humans; mammals; primates; vertebrates  
RN 9001-62-1 (LIPASE)  
20910-06-9D (CHOLESTERYL)

L24 ANSWER 6 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS  
AN 1995:477340 BIOSIS  
DN PREV199598491640  
TI Two polymorphic forms of human **lysosomal acid lipase** have different level of activity.

AU Du, Hong; Sheriff, Sulaiman  
CS Div. Human Genetics, Child. Hosp. Res. Found., Cincinnati, OH USA  
SO American Journal of Human Genetics, (1995) Vol. 57, No. 4 SUPPL., pp.  
A178.  
Meeting Info.: 45th Annual Meeting of the American Society of Human  
Genetics Minneapolis, Minnesota, USA October 24-28, 1995  
ISSN: 0002-9297.

DT Conference  
LA English  
IT Major Concepts  
Cardiovascular Medicine (Human Medicine, Medical Sciences);  
Development; Enzymology (Biochemistry and Molecular Biophysics);  
Genetics; Metabolism

IT Chemicals & Biochemicals  
LIPASE; CHOLESTERYL

IT Miscellaneous Descriptors  
**ATHEROSCLEROSIS; CHOLESTERYL ESTER**  
**STORAGE DISEASE; DELETION; HYPERLIPIDEMIA; INSERTION;**  
**MEETING ABSTRACT; MEETING POSTER; POINT MUTATION;**  
**WOLMAN DISEASE**

ORGN Super Taxa  
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name  
Hominidae (Hominidae)

ORGN Organism Superterms  
animals; chordates; humans; mammals; primates; vertebrates

RN 9001-62-1 (LIPASE)  
20910-06-9D (CHOLESTERYL)

L24 ANSWER 7 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS  
AN 1995:347392 BIOSIS  
DN PREV199598361692  
TI A novel variant of **lysosomal acid lipase**  
(Leu-336 fwdarw Pro) associated with acid lipase deficiency and  
**cholesterol ester storage disease**.  
AU Seedorf, Udo (1); Wiebusch, Heiko; Muntoni, Sandro; Christensen, Niels C.;  
Skovby, Flemming; Nickel, Volker; Roskos, Martin; Funke, Harald; Ose,  
Leiv; Assmann, Gerd  
CS (1) Inst. Arterioskleroseforschung Univ. Muenster, Domagkstr 3, 48149  
Muenster Germany  
SO Arteriosclerosis Thrombosis and Vascular Biology, (1995) Vol. 15, No. 6,  
pp. 773-778.  
ISSN: 1079-5642.

DT Article  
LA English  
AB **Cholesterol ester storage disease**  
(CESD) is associated with premature **atherosclerosis**,  
hepatomegaly, elevated LDL cholesterol levels, and in most cases, low HDL  
cholesterol levels. Previous studies have shown a G fwdarw A  
**mutation** at the 3' splice junction of exon 8 (E8SJM) of the gene  
encoding **lysosomal acid lipase** (LAL) in two  
kindreds with CESD. In a Canadian-Norwegian kindred with this disease, we  
show this **mutation** in conjunction with an as yet unknown T  
fwdarw C transition in exon 10 predicting a Leu-336 fwdarw Pro (L336P)  
replacement and an A fwdarw C transversion in exon 2 predicting a T-6P  
replacement in the prepeptide. Identification of the L336P rather than the  
T-6P replacement as the second defect underlying CESD in our patient is  
deduced from three lines of evidence. First, the E8SJM allele is located  
in cis with the **mutation** predicting the T-6P-encoding allele but  
in trans with the L336P-encoding allele; second, the L336P but not the  
T-6P replacement cosegregates with low LAL activity in the family; third,  
the T-6P replacement was found in 6 of 28 alleles from subjects with  
normal **lysosomal acid lipase** activity,

suggesting that this variant represents a frequent nonfunctional polymorphism. Since the residual LAL activity is higher and the clinical phenotype based on plasma lipid values and severity of hepatosplenomegaly is milder in this case than in a previously studied case who was homozygous for the E88JM allele, we conclude that the L336P variant appears to be associated with a phenotypically mild form of CESD.

IT Major Concepts  
 Enzymology (Biochemistry and Molecular Biophysics); Gastroenterology (Human Medicine, Medical Sciences); Genetics; Metabolism

IT Chemicals & Biochemicals  
 LIPASE; CHOLESTEROL

IT Miscellaneous Descriptors  
**ATHEROSCLEROSIS; GENETICS; LIVER DISEASE; LYSOSOMAL STORAGE DISEASE; PHENOTYPE**

ORGN Super Taxa  
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name  
 human (Hominidae)

ORGN Organism Superterms  
 animals; chordates; humans; mammals; primates; vertebrates

RN 9001-62-1 (LIPASE)  
 57-88-5D (CHOLESTEROL)

L24 ANSWER 8 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1995:61003 BIOSIS

DN PREV199598075303

TI End-Stage Renal Disease in a Patient with **Cholestry1 Ester Storage Disease** following Successful Liver Transplantation and Cyclosporine Immunosuppression.

AU Kale, S. Arundhati (1); Ferry, George D.; Hawkins, Edith P.  
 CS (1) Renal Section, Texas Children's Hosp., Houston, TX 77030 USA

SO Journal of Pediatric Gastroenterology and Nutrition, (1995) Vol. 20, No. 1, pp. 95-97.  
 ISSN: 0277-2116.

DT Article

LA English

IT Major Concepts

Cardiovascular Medicine (Human Medicine, Medical Sciences); Enzymology (Biochemistry and Molecular Biophysics); Gastroenterology (Human Medicine, Medical Sciences); Metabolism; Nutrition; Pharmacology; Physiology; Surgery (Medical Sciences); Urology (Human Medicine, Medical Sciences)

IT Chemicals & Biochemicals  
 CHOLESTERYL; CYCLOSPORINE; LIPASE

IT Miscellaneous Descriptors  
**ATHEROSCLEROSIS; CASE STUDY; CYCLOSPORINE; HYPERTENSION; IMMUNOSUPPRESSANT-DRUG; LYSOSOMAL ACID LIPASE DEFICIENCY; METABOLIC DISORDER**

ORGN Super Taxa  
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name  
 Hominidae (Hominidae)

ORGN Organism Superterms  
 animals; chordates; humans; mammals; primates; vertebrates

RN 20910-06-9D (CHOLESTERYL)  
 59865-13-3Q (CYCLOSPORINE)  
 63798-73-2Q (CYCLOSPORINE)  
 9001-62-1 (LIPASE)

L24 ANSWER 9 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1995:13655 BIOSIS

DN PREV199598027955

TI Molecular characterization of the underlying defects in two patients with

**cholesteryl ester storage disease.**

AU Seedorf, U. (1); Skovby, F.; Nickel, V. (1); Christensen, N. C.; Roskoss, M. (1); Brysch, P. (1); Ros, E.; Ose, L.; Assmann, G. (1)

CS (1) Inst. Arterioskleroseforschung, Muenster Germany

SO European Heart Journal, (1994) Vol. 15, No. ABSTR. SUPPL., pp. 419.

Meeting Info.: Joint XIIth World Congress of Cardiology and the XVIth Congress of the European Society of Cardiology Berlin, Germany September 10-14, 1994

ISSN: 0195-668X.

DT Conference

LA English

IT Major Concepts  
 Cardiovascular Medicine (Human Medicine, Medical Sciences); Enzymology (Biochemistry and Molecular Biophysics); Genetics; Metabolism

IT Chemicals & Biochemicals  
 CHOLESTERYL; LIPASE

IT Miscellaneous Descriptors  
**ATHEROSCLEROSIS; HYPERCHOLESTEROLEMIA; LYSOSOMAL ACID LIPASE; MEETING ABSTRACT; MEETING POSTER; WOLMAN DISEASE**

ORGN Super Taxa  
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name  
 human (Hominidae)

ORGN Organism Superterms  
 animals; chordates; humans; mammals; primates; vertebrates

RN 20910-06-9D (CHOLESTERYL)  
 9001-62-1 (LIPASE)

L24 ANSWER 10 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1993:288217 BIOSIS

DN PREV199345006342

TI Purification and characterization of human hepatic **lysosomal acid lipase**.

AU Ameis, Detlev (1); Merkel, Martin; Eckerskorn, Christoph; Greten, Heiner

CS (1) Dep. Med., Univ. Hamburg, Hamburg French Guiana

SO Circulation, (1992) Vol. 86, No. 4 SUPPL. 1, pp. I548.

Meeting Info.: 65th Scientific Sessions of the American Heart Association New Orleans, Louisiana, USA November 16-19, 1992

ISSN: 0009-7322.

DT Conference

LA English

IT Major Concepts  
 Cardiovascular Medicine (Human Medicine, Medical Sciences); Development; Enzymology (Biochemistry and Molecular Biophysics); Gastroenterology (Human Medicine, Medical Sciences); Genetics; Metabolism

IT Chemicals & Biochemicals  
 LIPASE; CHOLESTEROL

IT Miscellaneous Descriptors  
**ABSTRACT; ATHEROSCLEROSIS; CHOLESTEROL ESTER STORAGE DISEASE; LIPID METABOLISM; WOLMAN DISEASE**

ORGN Super Taxa  
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name  
 Hominidae (Hominidae)

ORGN Organism Superterms  
 animals; chordates; humans; mammals; primates; vertebrates

RN 9001-62-1 (LIPASE)  
 57-88-5D (CHOLESTEROL)

L24 ANSWER 11 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS

AN 1992:29287 BIOSIS  
 DN BA93:18562  
 TI DESCRIPTION OF A CASE OF CHOLESTERYL ESTER  
     STORAGE DISEASE WITH PREMATURE ATHEROSCLEROSIS

AU CUCHEL M; GIUDICI G A; PEROTTI M E; LONGI R; VERGANI C  
 CS ISTITUTO DI MEDICINA INTERNA UNIVERSITA DEGLI STUDI DI MILANO VIA PACE 9,  
     20122 MILANO, ITALY.  
 SO G ARTERIOSCLER, (1991) 16 (2), 97-102.  
 CODEN: GIARAS. ISSN: 0017-0224.

FS BA; OLD  
 LA Italian  
 AB The lysosomal theory of **atherosclerosis** suggests that altered lysosomal function might contribute to atherogenesis. Postmortem evidence of premature **atherosclerosis** in subjects with cholestryl ester shortage disease (CESD) support this theory. CESD is an inherited disease characterized by a defect of **lysosomal acid lipase** activity. We describe a 16-year old subject with clinical, laboratory, histochemical and ultrastructural data compatible with the diagnosis of CESD. In this subject B-mode ultrasound imaging identified an early atherosomatous lesion in the left common carotid artery. This finding provides further support for the lysosomal theory of **atherosclerosis**. Published studies suggest that reduced **lysosomal acid lipase** activity may represent an independent risk factor for premature development of **atherosclerosis**.

IT Miscellaneous Descriptors  
     HUMAN ADOLESCENT CAROTID ARTERY LESION LYSOSOMAL THEORY  
     LYSOSOMAL ACID LIPASE ACTIVITY DIAGNOSIS  
     HISTOCHEMISTRY

RN 9001-62-1 (LIPASE)  
     20910-06-9D (CHOLESTERYL)

L24 ANSWER 12 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS  
 AN 1991:466674 BIOSIS  
 DN BR41:92434  
 TI TREATMENT OF CHOLESTERYL ESTER STORAGE  
     DISEASE WITH COMBINED CHOLESTYRAMINE WITH LOVASTATIN.

AU MCCOY E; YOKOYAMA S  
 CS DEP. PEDIATRICS, FAC. MED., UNIV. ALBERTA, EDMONTON, ALBERTA, CAN.  
 SO WILLIAMS, C. L. AND E. L. WYNDER (ED.). ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, VOL. 623. HYPERLIPIDEMIA IN CHILDHOOD AND THE DEVELOPMENT OF ATHEROSCLEROSIS; MEETING, BETHESDA, MARYLAND, USA, MAY 2-4, 1990. X+482P. NEW YORK ACADEMY OF SCIENCES: NEW YORK, NEW YORK, USA. ILLUS. (1991) 0 (0), 453-454.  
 CODEN: ANYAA9. ISSN: 0077-8923. ISBN: 0-89766-658-5 (PAPER), 0-89766-657-7 (CLOTH).

DT Conference  
 FS BR; OLD  
 LA English  
 IT Miscellaneous Descriptors  
     HUMAN METABOLIC-DRUG GENETIC DISORDER LYSOSOMAL ACID  
     LIPASE DEFICIENCY ATHEROSCLEROSIS HYPERLIPIDEMIA

RN 9001-62-1 (LIPASE)  
     11041-12-6 (CHOLESTYRAMINE)  
     20910-06-9D (CHOLESTERYL)  
     75330-75-5 (LOVASTATIN)

L24 ANSWER 13 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS  
 AN 1990:519069 BIOSIS  
 DN BA90:136345  
 TI GENETIC LIPID STORAGE DISEASE WITH LYSOSOMAL ACID  
     LIPASE DEFICIENCY IN RATS.

AU YOSHIDA H; KURIYAMA M  
CS DEP. PATHOL., FAC. MED., KAGOSHIMA UNIV., KAGOSHIMA 890, JPN.  
SO LAB ANIM SCI, (1990) 40 (5), 486-489.  
CODEN: LBASAE. ISSN: 0023-6764.

FS BA; OLD  
LA English

AB We describe a new animal model of a genetic lipid storage disease analogous to human **Wolman's** disease. Affected Donryu rats, who inherited the disease in an autosomal recessive mode, manifested marked hepatosplenomegaly, lymph node enlargement, and thickened, dilated intestine. Morphologically, many characteristic foam cells were observed in livers and spleens. No adrenal calcification could be found in affected rats. Biochemical studies on spleen and liver tissues showed massive accumulation of esterified cholesterol and triglycerides, and deficiency of acid lipase for [14C]-cholesteryl oleate. This animal model could contribute greatly to the clarification of the physiological and pathological roles of **lysosomal acid lipase** in the metabolism of lipoproteins and cholesterol, and of the pathogenesis oftherosclerosis.

IT Miscellaneous Descriptors  
NEW ANIMAL MODEL HUMAN **WOLMAN'S** DISEASE AUTOSOMAL RECESSIVE INHERITANCE HEPATOSPLENOMEGLY LYMPH NODE ENLARGEMENT DILATED INTESTINE CHOLESTEROL TRIGLYCERIDES **ATHEROSCLEROSIS**

RN 57-88-5 (CHOLESTEROL)  
9001-62-1 (LIPASE)

L24 ANSWER 14 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS  
AN 1989:85564 BIOSIS  
DN BR36:41655

TI **CHOLESTERYL ESTER STORAGE DISEASE**  
RISK FACTORS FOR **ATHEROSCLEROSIS** IN A 15-YEAR-OLD BOY.

AU LONGHI R; VERGANI C; VALSASINA R; RIVA E; GALLUZZO C; AGOSTONI C;  
GIOVANNINI M

CS 5TH DEP. PEDIATRICS, INST. BIOMEDICAL SCI. 'OSPEDALE S. PAOLO', UNIV.  
MILAN, ITALY.

SO ANNUAL MEETING OF THE SOCIETY FOR THE STUDY OF INBORN ERRORS OF  
METABOLISM, SHEFFIELD, ENGLAND, UK, SEPTEMBER 22-25, 1987. J INHERITED  
METAB DIS. (1988) 11 (SUPPL 2), 143-145.  
CODEN: JIMDDP. ISSN: 0141-8955.

FS BR; OLD  
LA English

IT Miscellaneous Descriptors  
HUMAN CASE STUDY AUTOSOMAL RECESSIVE DISORDER **ATHEROSCLEROTIC**  
**RISK LYSOSOMAL ACID LIPASE**  
HYDROXYMETHYLGLUTARYL COENZYME A REDUCTASE SERUM CHOLESTEROL  
TRIGLYCERIDE HIGH-DENSITY LIPOPROTEINS

RN 57-88-5 (CHOLESTEROL)  
9001-62-1 (LIPASE)  
20910-06-9D (CHOLESTERYL)  
9028-35-7Q, 37250-24-1Q (HYDROXYMETHYLGLUTARYL COENZYME A REDUCTASE)

L24 ANSWER 15 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS  
AN 1987:41848 BIOSIS  
DN BA83:21194

TI GENETIC VARIATION OF HUMAN MONONUCLEAR LEUKOCYTE **LYSOSOMAL**  
**ACID LIPASE** ACTIVITY RELATIONSHIP TO  
**ATHEROSCLEROSIS**.

AU COATES P M; LANGER T; CORTNER J A  
CS LIPID-HEART RESEARCH CENTER, CHILDREN'S HOSPITAL PHILADELPHIA, DEP.  
PEDIATRICS, UNIV. PENNSYLVANIA SCH. MED., PHILADELPHIA, PA 19104, USA.

SO ATHEROSCLEROSIS, (1986) 62 (1), 11-20.  
CODEN: ATHSBL. ISSN: 0021-9150.

FS BA; OLD

LA English

AB Lysosomal acid lipase activity was measured in mononuclear leukocytes of patients selected on the basis of premature cardiovascular disease, with or without hyperlipidemia. Enzyme activity was significantly lower in the patient population (4.8 .+- . 1.3 nmol/min/mg protein, n = 190 males) than in an age-matched control population (5.4 .+- . 1.3 nmol/min/mg protein, n = 124 males). There was no effect of hypercholesterolemia or hypertriglyceridemia on the enzyme activity. In the group of patients with normal plasma lipids (n = 77), 18% had mononuclear leukocyte acid lipase activity which fell below the control population 5th percentile, and in the range of enzyme activity observed in cells from obligate heterozygotes for inherited acid lipase deficiency (**Wolman** disease and **cholesteryl ester storage disease**). Studies of acid lipase activity in families of our patients provided evidence that an autosomal mutation is associated with (or responsible for) this reduced enzymatic activity and may represent an independent risk factor for the premature development of **atherosclerosis**.

IT Miscellaneous Descriptors

WOLMAN DISEASE CHOLESTERYL ESTER  
STORAGE DISEASE AUTOSOMAL MUTATION

RN 9001-62-1 (LIPASE)  
20910-06-9D (CHOLESTERYL)

=> fil medlins  
'MEDLINS' IS NOT A VALID FILE NAME  
SESSION CONTINUES IN FILE 'MEDLINE'

=> fil medline  
FILE 'MEDLINE' ENTERED AT 12:42:28 ON 18 OCT 2001

FILE LAST UPDATED: 17 OCT 2001 (20011017/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

'MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

MEDLINE is now updated 4 times per week. A new current-awareness alert frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> d his

(FILE 'BIOSIS' ENTERED AT 12:27:16 ON 18 OCT 2001)  
DEL HIS Y

FILE 'MEDLINE' ENTERED AT 12:28:22 ON 18 OCT 2001

FILE 'REGISTRY' ENTERED AT 12:28:26 ON 18 OCT 2001  
E LYSOSOMAL ACID LIPASE/CN

L1 1 S E3

FILE 'MEDLINE' ENTERED AT 12:28:37 ON 18 OCT 2001

L2 0 S L1  
E LYSOSOMAL ACID LIPASE  
L3 118 S LYSOSOMAL ACID LIPASE  
L4 1291 S ESTERASE (2A) CHOLESTEROL? OR CHOLESTERASE# OR CHOLESTERIN ES  
L5 150 S LYSOSOMAL ACID LIPASE# OR STEROL (W) (ESTER HYDROLASE# OR EST  
L6 1396 S L4 OR L5  
E ATHEROSCLEROSIS/CT  
E E3+ALL  
E E2+ALL  
L7 0 S ARTERIOSCLEROSIS+NT/CT  
L8 56249 S ARTERIOSCLEROSIS+NT/CT  
L9 84 S L8 AND L6  
L10 145693 S PLASMID# OR VECTOR?  
L11 0 S L9 AND L10  
L12 0 S MANNOSE AND L9  
L13 17548 S ARTERIOSCLEROSIS+NT/CT (L) TH./CT  
L14 15 S L9 AND L13  
E ANTIARTERIOSCLERO/CT  
E ANTIARTERIOSCLER?  
E ANTIARTHERIOSCLER?  
L15 29 S ANTIARTERIOS?

E ANTIIDIPEMIC AGENTS/CT  
 E E3+ALL  
 L16 4818 S ANTIIDIPEMIC AGENTS/CT OR ANTICHOESTEREMIC AGENTS/CT  
 L17 10043 S L16 OR ANTICHOESTEREMIC AGENTS/CT  
 L18 5 S L17 AND L9  
 L19 16 S L14 OR L18  
 L20 7976 S DRUG DELIVER?  
 L21 0 S L9 AND L20  
 L22 165186 S DELIVER?  
 L23 0 S L9 AND L21  
 L24 0 S ACETYGLYCOSYLAT? AND L9  
 E WOLMAN /CT  
 E E5+ALL  
 L25 85 S WOLMAN DISEASE/CT  
 L26 65 S CHOLESTEROL ESTER STORAGE DISEASE+NT/CT  
 L27 132 S L25 OR L26  
 L28 2 S L27 AND L9  
 L29 17 S L19 OR L28

FILE 'MEDLINE' ENTERED AT 12:42:28 ON 18 OCT 2001

=> d .med 1-17

L29 ANSWER 1 OF 17 MEDLINE  
 AN 2001295567 MEDLINE  
 DN 21273916 PubMed ID: 11380065  
 TI Long-term administration of the HMG-CoA reductase inhibitor lovastatin in  
 two patients with cholestrylo ester storage disease.  
 AU Rassoul F; Richter V; Lohse P; Naumann A; Purschwitz K; Keller E  
 CS Department of Clinical Chemistry and Pathobiochemistry, University  
 Leipzig/Working Group Health Promotion and Prevention of Atherosclerosis  
 (AGA), Germany.. rassf@medizin.uni-leipzig.de  
 SO INTERNATIONAL JOURNAL OF CLINICAL PHARMACOLOGY AND THERAPEUTICS, (2001  
 May) 39 (5) 199-204.  
 Journal code: BOD; 9423309. ISSN: 0946-1965.  
 CY Germany: Germany, Federal Republic of  
 DT (CLINICAL TRIAL)  
 Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200110  
 ED Entered STN: 20011008  
 Last Updated on STN: 20011008  
 Entered Medline: 20011004  
 AB OBJECTIVE: In order to suppress de novo cholesterol and VLDL biosynthesis,  
 a long-term therapy trial with lovastatin, a competitive inhibitor of  
 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, was initiated  
 in two patients with cholestrylo ester storage disease (CESD), and  
 concentrations of plasma lipids were monitored over a period of 9 years.  
 METHODS: We studied two male patients with enzymatically confirmed CESD in  
 whom long-term lovastatin therapy (8 and 9 years) was begun at the age of  
 7 and 19 years. The diagnosis of CESD was confirmed by the measurement of  
 human lysosomal acid lipase (hLAL) activity  
 in cultured skin fibroblasts and leukocytes. Restriction fragment length  
 polymorphism (RFLP) analysis revealed that both subjects are homozygotes  
 for the common CESD splice site mutation. Levels of serum lipids and  
 lipoproteins were measured yearly. RESULTS: During the first year, total  
 serum cholesterol decreased from 317 to 201 mg/dl in Patient A and from  
 228 to 120 mg/dl in Patient B, due mainly to the reduction of low-density  
 lipoprotein (LDL) cholesterol from 262 to 151 mg/dl in Patient A and from  
 166 to 66 mg/dl in Patient B. Accordingly, the LDL cholesterol : high  
 density lipoprotein (HDL) cholesterol ratio was markedly reduced in both  
 patients after one year of therapy. The treatment was continued and, after

9 years of further medication, low total cholesterol and LDL cholesterol levels were still maintained. CONCLUSIONS: The study demonstrates that HMG-CoA reductase inhibitors are well tolerated drugs during long-term treatment of CESD patients and may help to prevent the development of premature atherosclerosis.

CT Check Tags: Human; Male  
 Adult  
**Arteriosclerosis: PC, prevention & control**  
 Child  
 \*Cholesterol: BL, blood  
**Cholesterol Ester Storage Disease: BL, blood**  
**\*Cholesterol Ester Storage Disease: DT, drug therapy**  
**Cholesterol Ester Storage Disease: GE, genetics**  
 Drug Administration Schedule  
**\*Hydroxymethylglutaryl-CoA Reductase Inhibitors: TO, toxicity**  
 Longitudinal Studies  
 Polymorphism, Restriction Fragment Length  
 \*Triglycerides: BL, blood

L29 ANSWER 2 OF 17 MEDLINE  
 AN 2000197673 MEDLINE  
 DN 20197673 PubMed ID: 10735626  
 TI Subclinical course of cholestrylo ester storage disease in an adult with hypercholesterolemia, accelerated atherosclerosis, and liver cancer.  
 AU Elleder M; Chlumska A; Hynek J; Poupetova H; Ledvinova J; Maas S; Lohse P  
 CS Institute of Inherited Metabolic Disorders, Charles University Prague, 1st Faculty of Medicine and General Faculty Hospital, Praha, Czech Republic..  
 melleder@beba.cesnet.cz  
 SO JOURNAL OF HEPATOLOGY, (2000 Mar) 32 (3) 528-34.  
 Journal code: IBS; 8503886. ISSN: 0168-8278.  
 CY Denmark  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 200004  
 ED Entered STN: 20000421  
 Last Updated on STN: 20000421  
 Entered Medline: 20000412  
 AB Few cases of asymptomatic cholestrylo ester storage disease (CESD) due to low enzymatic activity of human **lysosomal acid lipase/cholesteryl ester hydrolase** (hLAL) have been reported thus far in adults. Here, we describe a 51-year-old man with a long clinical history of mixed hyperlipoproteinemia and severe premature atherosclerosis, but with no signs of hepatomegaly, liver dysfunction, or splenomegaly. The disease was discovered by chance in a biopsy performed because of suspected liver cancer (proven to be a cholangiocarcinoma). Residual hLAL activity in peripheral leukocytes was determined to be 6% of control values. DNA sequence and restriction fragment length polymorphism analysis demonstrated that the patient was a compound heterozygote for the prevalent CESD exon 8 splice site mutation (G934A) and the deletion of a C (nucleotide 673, 674, or 675) in exon 6 of the hLAL gene, resulting in premature termination of protein translation at residue 195. The patient died of liver failure as a consequence of extensive tumor infiltration at age 52. Lipid analysis revealed moderate cholestrylo ester storage in the liver and in the suprarenal cortex, and massive accumulation in the testicular histiocytes and Leydig cells, resulting in a pronounced secondary atrophy of the seminiferous tubules. Our case study demonstrates that hepatomegaly is an inconstant feature, even in CESD patients compound heterozygous for a Wolman mutation which results in complete loss of hLAL enzymic activity. It also highlights the need to be aware of this condition as it may be underdiagnosed.  
 CT Check Tags: Case Report; Human; Male; Support, Non-U.S. Gov't  
 Adult

\*Arteriosclerosis: CO, complications  
Base Sequence: GE, genetics  
\*Cholesterol Ester Storage Disease: CO, complications  
Cholesterol Ester Storage Disease: GE, genetics  
\*Cholesterol Ester Storage Disease: PP, physiopathology  
DNA: GE, genetics  
\*Hypercholesterolemia: CO, complications  
Liver: ME, metabolism  
Liver: PA, pathology  
\*Liver Neoplasms: CO, complications  
Pedigree  
Polymorphism, Restriction Fragment Length

L29 ANSWER 3 OF 17 MEDLINE  
AN 97417030 MEDLINE  
DN 97417030 PubMed ID: 9270979  
TI Effect of trifluoperazine on certain arterial wall lipid-metabolizing enzymes inducing atherosclerosis in rhesus monkeys.  
AU Mohindroo A; Ahluwalia P  
CS Department of Biochemistry, Panjab University, Chandigarh, India.  
SO LIPIDS, (1997 Aug) 32 (8) 867-72.  
Journal code: L73; 0060450. ISSN: 0024-4201.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 199710  
ED Entered STN: 19971024  
Last Updated on STN: 19980206  
Entered Medline: 19971014  
AB The effect of trifluoperazine (TFP) was investigated on arterial wall lipid-metabolizing enzymes like acyl-CoA:cholesterol acyltransferase (ACAT) and cholesterol ester hydrolase (CEH) in rhesus monkeys. The activity was determined in aortic wall homogenates obtained from rhesus monkeys fed an atherogenic diet coupled with intramuscular injections of adrenaline and TFP. Although TFP had no significant effect on serum cholesterol and triglycerides, it decreased significantly the formation of atherosclerotic lesions by decreasing the esterification of cholesterol, by inhibiting ACAT and enhancing its utilization by activating CEH. Hence, the preventive effect of TFP on the development of atherosclerosis in rhesus monkeys is mediated through its ability to influence the activities of arterial wall lipid-metabolizing enzymes like ACAT and CEH.  
CT Check Tags: Animal; Male  
Aorta: DE, drug effects  
\*Aorta: EN, enzymology  
Aorta: ME, metabolism  
    Arteriosclerosis: ET, etiology  
    \*Arteriosclerosis: PC, prevention & control  
Blood Pressure: DE, drug effects  
Cholesterol: BL, blood  
    \*Cholesterol Esterase: ME, metabolism  
Cholesterol Esters: ME, metabolism  
Diet, Atherogenic  
Epinephrine: PD, pharmacology  
Hypercholesterolemia: EN, enzymology  
\*Lipids: ME, metabolism  
Lipoproteins: BL, blood  
Macaca mulatta  
Muscle, Smooth, Vascular: DE, drug effects  
Muscle, Smooth, Vascular: EN, enzymology  
\*Sterol O-Acyltransferase: AI, antagonists & inhibitors  
\*Trifluoperazine: PD, pharmacology

Trifluoperazine: TU, therapeutic use  
 Triglycerides: BL, blood

L29 ANSWER 4 OF 17 MEDLINE  
 AN 97043963 MEDLINE  
 DN 97043963 PubMed ID: 8889034  
 TI Anti-hyperlipidemic and anti-atherosclerotic actions of shosaikoto (kampo medicine).  
 AU Shen Y R; Inoue M; Nagatsu Y; Ogihara Y; Aburada M  
 CS Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Nagoya City University, Japan.  
 SO BIOLOGICAL AND PHARMACEUTICAL BULLETIN, (1996 Sep) 19 (9) 1160-5.  
 Journal code: BPZ; 9311984. ISSN: 0918-6158.  
 CY Japan  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199702  
 ED Entered STN: 19970306  
 Last Updated on STN: 19980206  
 Entered Medline: 19970224  
 AB We investigated the anti-atherosclerotic action shown by Shosaikoto, a Kampo medicine, using hypercholesterolemic mice. Oral administration of Shosaikoto significantly suppressed the elevation of serum cholesterol in C57BL/6 mice fed a 1.25% cholesterol-enriched diet for four weeks and improved the T cell ratio in peripheral blood, which decreased with the increase of the serum cholesterol level. In addition, Shosaikoto reduced the accumulation of cholesteryl oleate, which alters macrophages into foam cells, after the treatment of macrophages with oxidized or acetylated low density lipoprotein (LDL). Enzymatic study revealed that the treatment of macrophages with oxidized LDL enhanced acyl-coenzyme A: cholesterol acyltransferase (ACAT) activity and markedly reduced neutral cholesteryl ester hydrolase (NCEase) activity. Shosaikoto treatment prevented a decrease in the NCEase activity, however due to the oxidized LDL treatment, although it slightly augmented ACAT activity. Thus, Shosaikoto, which is known to modulate the immune system, improves macrophage and lymphocyte functions diminished by hypercholesterolemia, resulting in an anti-atherosclerotic action.  
 CT Check Tags: Animal; Male  
   \*Anticholesteremic Agents: PD, pharmacology  
   Anticholesteremic Agents: TU, therapeutic use  
   \*Antilipemic Agents: PD, pharmacology  
   \*Arteriosclerosis: DT, drug therapy  
   Cholesterol Esterase: ME, metabolism  
   Cholesterol Esters: BL, blood  
   Cholesterol Esters: ME, metabolism  
   \*Drugs, Chinese Herbal: PD, pharmacology  
   Drugs, Chinese Herbal: TU, therapeutic use  
   Flow Cytometry  
   Fluorescent Antibody Technique, Indirect  
   Lipoproteins, HDL: BL, blood  
   Lipoproteins, LDL: BL, blood  
   Macrophages, Peritoneal: DE, drug effects  
   Macrophages, Peritoneal: EN, enzymology  
   Macrophages, Peritoneal: ME, metabolism  
   Mice  
   Mice, Inbred C57BL  
   Sterol O-Acyltransferase: BL, blood

L29 ANSWER 5 OF 17 MEDLINE  
 AN 95067601 MEDLINE  
 DN 95067601 PubMed ID: 7977012  
 TI Calcium channel blockers and coronary atherosclerosis: from the rabbit to

the real world.

AU Waters D; Lesperance J  
 CS Division of Cardiology, Hartford Hospital, CT 06102-5037.  
 SO AMERICAN HEART JOURNAL, (1994 Dec) 128 (6 Pt 2) 1309-16. Ref: 48  
 Journal code: 3BW; 0370465. ISSN: 0002-8703.

CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 (REVIEW, TUTORIAL)

LA English  
 FS Abridged Index Medicus Journals; Priority Journals  
 EM 199412  
 ED Entered STN: 19950110  
 Last Updated on STN: 19950110  
 Entered Medline: 19941227

AB Many calcium channel blockers have been shown to retard the development of atherosclerosis in cholesterol-fed rabbits. The mechanisms that may contribute to this effect include stimulation of **cholesteryl ester hydrolase** activity in smooth muscle cells, amelioration of hypercholesterolemic-induced endothelial dysfunction, or inhibition of smooth muscle cell proliferation and migration. The effect of calcium channel blockers on the evolution of coronary atherosclerosis in humans has been assessed in three clinical trials. In the Montreal Heart Institute trial, nicardipine did not influence the overall rate of progression and regression; however, patients treated with nicardipine experienced significantly less progression of minimal lesions, defined as stenoses of less than or equal to 20% severity. In the International Nifedipine Trial on Antiatherosclerotic Therapy (INTACT), nifedipine had no effect on overall progression and regression but, by one method of analysis, reduced the rate of appearance of new coronary lesions. In a preliminary report, diltiazem prevented the development of coronary atherosclerosis in heart transplant recipients. These studies indicate that calcium channel blockers retard the development of early atherosclerosis not only in animal models but also in human coronary arteries. Other studies recently completed or now under way will help to clarify the clinical role of calcium channel blockers in antiatherosclerotic therapy.

CT Check Tags: Animal; Human  
 Calcium Channel Blockers: PD, pharmacology  
 \*Calcium Channel Blockers: TU, therapeutic use  
 Clinical Trials  
 \*Coronary Arteriosclerosis: DT, drug therapy  
 Disease Models, Animal  
 Drug Evaluation, Preclinical  
 Heart Transplantation  
 Rabbits

L29 ANSWER 6 OF 17 MEDLINE  
 AN 93217620 MEDLINE  
 DN 93217620 PubMed ID: 1297739  
 TI Atherosclerosis from a viewpoint of arterial wall cell function: relation to vitamin E.  
 AU Morisaki N; Yokote K; Saito Y  
 CS Second Department of Internal Medicine, School of Medicine, Chiba University, Japan.  
 SO JOURNAL OF NUTRITIONAL SCIENCE AND VITAMINOLOGY, (1992) Spec No 196-9.  
 Journal code: JFD; 0402640. ISSN: 0301-4800.

CY Japan  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199305  
 ED Entered STN: 19930521

Last Updated on STN: 19930521

Entered Medline: 19930504

AB Vitamin E affects many key events in atherosomatous lesions. Inhibition of EC injury and platelet aggregation was already reported.. Foam cell formation must be inhibited according to the data presented by us and other speakers. However, effects on cell proliferation of SMC are paradoxical. The in vivo effects will be dependent on the effective concentration of vitamin E in the loci.

CT Check Tags: Animal; Comparative Study; Male

Arteries

Arteriosclerosis: ME, metabolism

\*Arteriosclerosis: PC, prevention &amp; control

Cell Adhesion: DE, drug effects

Cholesterol Esterase: DE, drug effects

\*Endothelium, Vascular: DE, drug effects

Endothelium, Vascular: EN, enzymology

Endothelium, Vascular: ME, metabolism

Free Radical Scavengers

Monocytes: CY, cytology

Muscle, Smooth, Vascular: CY, cytology

Muscle, Smooth, Vascular: DE, drug effects

Rats

Rats, Wistar

\*Vitamin E: PD, pharmacology

Vitamin E Deficiency: ME, metabolism

L29 ANSWER 7 OF 17 MEDLINE

AN 93047191 MEDLINE

DN 93047191 PubMed ID: 1424044

TI Interventions that beneficially influence the evolution of coronary atherosclerosis. The case for calcium channel blockers.

AU Waters D; Lesperance J

CS Department of Medicine, Montreal Heart Institute, Quebec, Canada.

SO CIRCULATION, (1992 Dec) 86 (6 Suppl) III111-6. Ref: 55  
Journal code: DAW; 0147763. ISSN: 0009-7322.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 199212

ED Entered STN: 19930122

Last Updated on STN: 19930122

Entered Medline: 19921223

AB Calcium channel blockers have been shown to retard the development of atherosclerosis in rabbits fed cholesterol-rich diets. The mechanism accounting for this effect is controversial but may be by stimulation of **cholesteryl ester hydrolase** activity in smooth muscle cells, by amelioration of hypercholesterolemia-induced endothelial dysfunction, or by inhibition of smooth muscle cell proliferation and migration. The effect of calcium channel blockers on the evolution of coronary atherosclerosis in humans has been assessed in two clinical trials. In the Montreal Heart Institute trial, nifedipine did not influence the overall rate of progression and regression; however, nifedipine-treated patients experienced significantly less progression of minimal lesions, defined as stenoses of < or = 20% severity. In the International Nifedipine Trial on Antiatherosclerotic Therapy, nifedipine had no effect on overall progression and regression but reduced the rate of appearance of new coronary lesions. These studies constitute a potentially important new approach to the management of coronary atherosclerosis.

CT Check Tags: Animal; Human

\*Calcium Channel Blockers: TU, therapeutic use  
 Coronary Arteriosclerosis: PC, prevention & control  
 Coronary Arteriosclerosis: SU, surgery  
 \*Coronary Arteriosclerosis: TH, therapy  
 Disease Models, Animal  
 Heart Transplantation  
 Nifedipine: TU, therapeutic use  
 Rabbits  
 Randomized Controlled Trials

L29 ANSWER 8 OF 17 MEDLINE  
 AN 91063673 MEDLINE  
 DN 91063673 PubMed ID: 2248458  
 TI Clinical and experimental approaches to the prevention of atherosclerosis by immunological regulations.  
 AU Kuzuya F; Kuzuya M; Yasue M; Naito M; Funaki C; Hayashi T; Asai K  
 CS Department of Geriatrics, Nagoya University School of Medicine, Japan.  
 SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1990) 598 458-63.  
 Journal code: 5NM; 7506858. ISSN: 0077-8923.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 199101  
 ED Entered STN: 19910222  
 Last Updated on STN: 19910222  
 Entered Medline: 19910110  
 AB To evaluate the involvement of the complement system in atherogenesis, we investigated the effect of camostat mesilate (CM), Clr, and C1 esterase inhibitor on cholesterol-induced atherosclerosis in rabbits. We also examined the effect of sodium dextran sulfate (DS, molecular weight: 7000), which is reported to be effective in preventing arteriosclerotic diseases and in inhibiting cholesterol-induced atherosclerosis in experimental animals, on complement activation in vitro and in vivo. The administration of CM reduced the formation of atherosclerotic lesions in cholesterol-fed rabbits. DS inhibited complement pathway in vitro, and the administration of DS reduced the C3a level in subjects. These results suggest that complement activation may possibly be involved in the atherosclerotic process.

CT Check Tags: Animal; Female; Human; Male  
 Aged  
 Arteriosclerosis: ET, etiology  
 \*Arteriosclerosis: PC, prevention & control  
 \*Complement: PH, physiology  
 Complement Activation: DE, drug effects  
 Dextran Sulfate: PD, pharmacology  
 Guanidines: PD, pharmacology  
 Middle Age  
 Rabbits

L29 ANSWER 9 OF 17 MEDLINE  
 AN 89392166 MEDLINE  
 DN 89392166 PubMed ID: 2783199  
 TI Protective effect of BN 52021, a specific antagonist of platelet-activating factor (PAF-acether) against diet-induced cholestrylo ester deposition in rabbit aorta.  
 AU Feliste R; Perret B; Braquet P; Chap H  
 CS INSERM Unite 101, Hopital Purpan, Toulouse, France.  
 SO ATHEROSCLEROSIS, (1989 Aug) 78 (2-3) 151-8.  
 Journal code: 95X; 0242543. ISSN: 0021-9150.  
 CY Netherlands  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English

FS Priority Journals  
 EM 198910  
 ED Entered STN: 19900309  
 Last Updated on STN: 19980206  
 Entered Medline: 19891026  
 AB Platelet-activating factor (PAF-acether), a phospholipid mediator involved in inflammatory reactions, has been reported to induce endovascular surface lesions. We investigated the possible involvement of PAF-acether in the mechanism of arterial cholesterol deposition. Rabbits fed a normal or hypercholesterolic diet were treated orally for 1 month with BN 52021 (20 mg/kg per day), a specific PAF-acether antagonist, and killed at the end of treatment. Cholesterol feeding resulted in a marked (50-fold) increase in plasma cholesterol. However, the drug had no significant effect on the diet-induced hypercholesterolemia. Free and esterified cholesterol were markedly increased (635%) in the aorta of animals receiving the atherogenic diet. This accumulation was reduced by 36% upon simultaneous administration of BN 52021 ( $P < 0.02$ ,  $n = 15$ ). This decrease essentially affected the esterified cholesterol content. Conversely, BN 52021 showed no effect on the cellular cholesterol esterification, since liver acyl-CoA: cholesterol acyltransferase activity remained unchanged. This study indicates that BN 52021 is effective in reducing cholesterol accumulation in rabbit atherosclerotic aorta, without changing the plasma cholesterol levels.  
 CT Check Tags: Animal  
     \*Aorta: ME, metabolism  
     Aorta: PA, pathology  
     \*Arteriosclerosis: PC, prevention & control  
     Cholesterol: BL, blood  
     Cholesterol Esterase: ME, metabolism  
     \*Cholesterol Esters: ME, metabolism  
     Diet, Atherogenic  
     \*Lactones: PD, pharmacology  
     \*Platelet Activating Factor: AI, antagonists & inhibitors  
     Platelet Aggregation: DE, drug effects  
     Rabbits  
     Sterol O-Acyltransferase: ME, metabolism  
  
 L29 ANSWER 10 OF 17 MEDLINE  
 AN 88049134 MEDLINE  
 DN 88049134 PubMed ID: 3675303  
 TI Fish oil inhibits development of atherosclerosis in rhesus monkeys.  
 AU Davis H R; Bridenstine R T; Vesselinovitch D; Wissler R W  
 CS Department of Pathology, University of Chicago, Illinois.  
 NC HL 36104 (NHLBI)  
     HL-15062 (NHLBI)  
 SO ARTERIOSCLEROSIS, (1987 Sep-Oct) 7 (5) 441-9.  
     Journal code: 89S; 8401388. ISSN: 0276-5047.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198711  
 ED Entered STN: 19900305  
 Last Updated on STN: 19980206  
 Entered Medline: 19871127  
 AB The effect of feeding fish oil (Menhaden) on the progression of rhesus monkey atherosclerosis was determined by feeding diets containing 2% cholesterol and either 25% coconut oil (Group I), 25% fish oil/coconut oil (1:1) (Group II), or 25% fish oil/coconut oil (3:1) (Group III) for 12 months ( $n = 8$ /group). The average serum cholesterol levels were 875 mg/dl for Group I, 463 mg/dl for Group II, and 405 mg/dl for Group III. HDL cholesterol levels were 49 mg/dl for Group I, 29 mg/dl for Group II, and 20 mg/dl for Group III. An average of 79% of the aortic intima was

involved with atherosclerosis in Group I, 48% in Group II, and 36% in Group III. The aortas of both fish-oil groups (II or III) contained significantly less cholesterol (total, free, and esterified), as well as less acid lipase, **cholesteryl esterase**, and ACAT activities when compared to the coconut-oil group (I) (*p* less than 0.05). Microscopically, the aortic and carotid artery lesions were smaller in cross-sectional area and in thickness, and contained less macrophages in the fish-oil groups (II and III) when compared to the coconut-oil group (I) (*p* less than 0.05). This protective effect was not consistently enhanced by increasing the proportion of fish oil to 3:1 (Group III) over 1:1 (Group II). The results indicate that fish oil-containing diets reduce serum cholesterol levels and inhibit atherosclerosis even in the face of lowered HDL cholesterol levels when compared to a pure coconut oil/cholesterol diet in rhesus monkeys. Therefore, fish-oil diets exert effective protective control of progression of atherosclerosis during severe atherogenic stimuli.

CT Check Tags: Animal; Comparative Study; Male; Support, U.S. Gov't, P.H.S.

Aorta: PA, pathology

**Arteriosclerosis: PA, pathology**

\***Arteriosclerosis: PC, prevention & control**

Carotid Arteries: PA, pathology

Cholesterol, Dietary: AD, administration & dosage

Diet, Atherogenic

Dietary Fats: AD, administration & dosage

\***Fish Oils: AD, administration & dosage**

Lipoproteins, HDL Cholesterol: BL, blood

Macaca mulatta

Sterol O-Acyltransferase: ME, metabolism

Time Factors

L29 ANSWER 11 OF 17 MEDLINE

AN 85208364 MEDLINE

DN 85208364 PubMed ID: 3923040

TI Nifedipine increases cholesteryl ester hydrolytic activity in lipid-laden rabbit arterial smooth muscle cells. A possible mechanism for its antiatherogenic effect.

AU Etingin O R; Hajjar D P

NC 5-TH (NHLBI)

HL-074423 (NHLBI)

HL-07423 (NHLBI)

HL-18828

SO JOURNAL OF CLINICAL INVESTIGATION, (1985 May) 75 (5) 1554-8.

Journal code: HS7; 7802877. ISSN: 0021-9738.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Abridged Index Medicus Journals; Priority Journals

EM 198507

ED Entered STN: 19900320

Last Updated on STN: 19970203

Entered Medline: 19850703

AB Calcium and cholesterol (CHOL) accumulation are characteristic features of human atherosclerotic plaques. Calcium channel blockers have been shown to increase calcium levels in myocardial cells and suppress free and esterified CHOL deposition in arteries of CHOL-fed animals. To test the hypothesis that Nifedipine alters CHOL metabolism, thereby decreasing free and esterified CHOL accumulation in smooth muscle cells (SMC), we cultured arterial SMC from rabbits fed a normal or egg-supplemented diet for 6 mo. Cultured cells were treated with 0.1 mg/liter Nifedipine every 3 d during a 1-wk experiment. Although Nifedipine significantly increased lysosomal and cytoplasmic cholesteryl ester (CE) hydrolase activity in normal SMC via increased levels of intracellular cyclic AMP, no change in total CHOL content was observed after 1 wk of Nifedipine treatment. Contrary to these

observations, lipid-laden SMC demonstrated a significant 50% loss in CHOL and CE after treatment with Nifedipine, due in part to the observed increase in CE hydrolytic activities. These data support our hypothesis that Nifedipine decreases CHOL and CE accumulation in arterial SMC by increasing arterial CE hydrolysis.

CT Check Tags: Animal; Female; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

\*Arteriosclerosis: DT, drug therapy

Cattle

Cells, Cultured

\*Cholesterol: ME, metabolism

Cholesterol Esterase: ME, metabolism

\*Cholesterol Esters: ME, metabolism

Cholesterol, Dietary: AD, administration & dosage

Lysosomes: EN, enzymology

Muscle, Smooth, Vascular: CY, cytology

\*Muscle, Smooth, Vascular: ME, metabolism

\*Nifedipine: PD, pharmacology

Rabbits

beta-Galactosidase: ME, metabolism

L29 ANSWER 12 OF 17 MEDLINE

AN 85148553 MEDLINE

DN 85148553 PubMed ID: 6680996

TI Effect of clinofibrate on lipid metabolism of aorta in atherosclerotic rats.

AU Shirai K; Ishikawa Y; Nishide T; Sasaki N; Murano S; Matsuoka N; Saito Y; Yoshida S

SO ARTERY, (1983) 12 (3) 145-55.

Journal code: 8NN; 7508494. ISSN: 0098-6127.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 198504

ED Entered STN: 19900320

Last Updated on STN: 19900320

Entered Medline: 19850410

AB Atherosclerotic lesions formed in the aorta of rats given diet containing propylthiouracil (PTU), vitamin D2 and high cholesterol diet (atherogenic) for 8 weeks. The effect of clinofibrate, which lowers the plasma lipid level, on lipid metabolism in the arterial wall of the atherosclerotic rats was studied. Clinofibrate significantly decreased the high plasma cholesterol level of atherosclerotic rats, which was  $823 \pm 256$  (mean  $\pm$  SD) mg/dl, or about ten times that of control rats ( $85 \pm 11$  mg/dl). On treatment with clinofibrate, the cholesterol level was reduced most in the very low density lipoprotein (VLDL) fraction (d less than 1.006). Heparin-releasable lipoprotein lipase activity in epididymal adipose tissue, lipoprotein lipase activity in post heparin plasma, and VLDL-triolein hydrolyzing activity in adipose tissue stromal vessels were higher in clinofibrate-treated rats than in atherosclerotic rats. Of the enzymes in the arterial wall concerned with cholesterol ester metabolism, acid cholesterol esterase activity was decreased in atherosclerotic rats, and clinofibrate treatment increased this activity. The ratio of acyl-CoA cholesterol acyltransferase activity (ACAT) to neutral cholesterol esterase activity was higher in atherosclerotic rats than in control rats and was lower in clinofibrate-treated rats than in atherosclerotic rats. From these results, it is concluded that clinofibrate modifies enzyme activities in such a way as to cause a reduction of cholesterol accumulation in the arterial wall and lowers the plasma VLDL and LDL cholesterol levels.

CT Check Tags: Animal; Comparative Study; Male

Antilipemic Agents: PD, pharmacology

\*Aorta: DE, drug effects  
 Aorta: ME, metabolism  
 \*Arteriosclerosis: DT, drug therapy  
 Arteriosclerosis: ME, metabolism  
 Cholesterol Esters: ME, metabolism  
 \*Glycolates: PD, pharmacology  
 \*Lipids: ME, metabolism  
 Lipoprotein Lipase: ME, metabolism  
 \*Phenoxyacetates: PD, pharmacology  
 Rats  
 Rats, Inbred Strains

L29 ANSWER 13 OF 17 MEDLINE  
 AN 84272959 MEDLINE  
 DN 84272959 PubMed ID: 6463093  
 TI Influence of hypocholesterolemic drugs on aortic **cholesterol esterase** in rabbits.  
 AU Kritchevsky D; Singer D; Klurfeld D M  
 NC HL-00734 (NHLBI)  
 HL-03299 (NHLBI)  
 HL-23625 (NHLBI)  
 SO PHARMACOLOGICAL RESEARCH COMMUNICATIONS, (1984 Jun) 16 (6) 525-31.  
 Journal code: P3W; 0236354. ISSN: 0031-6989.  
 CY United States  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198408  
 ED Entered STN: 19900320  
 Last Updated on STN: 19970203  
 Entered Medline: 19840824  
 AB We have studied the influence of three hypocholesterolemic drugs (Fenofibrate, Pirinixil and Probucol) on aortic **cholesterol esterase** (E.C.3.1.1.13) activity in cholesterol-fed rabbits. After three weeks, cholesterol-fed controls exhibited a 28% increase in cholesteryl ester synthetase activity (S) and a 13% decrease in cholesteryl ester hydrolase activity (H) giving a 47% increase in S/H ratio. None of the drugs influenced cholesterol-induced synthetase activity, but fenofibrate treatment increased hydrolase activity resulting in a fall in the S/H ratio to the level observed in rabbits fed corn oil but no cholesterol. The other two hypocholesterolemic agents did not affect the aortic S/H ratio.  
 CT Check Tags: Animal; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't,  
 P.H.S.  
 \*Anticholesteremic Agents: PD, pharmacology  
 \*Aorta: EN, enzymology  
 Arteriosclerosis: ET, etiology  
 Arteriosclerosis: PC, prevention & control  
 \*Carboxylic Ester Hydrolases: ME, metabolism  
 Cholesterol: BL, blood  
 \*Cholesterol Esterase: ME, metabolism  
 Cholesterol, Dietary: AD, administration & dosage  
 Diet, Atherogenic  
 Probucol: PD, pharmacology  
 Procetofen: PD, pharmacology  
 Pyrimidines: PD, pharmacology  
 Rabbits  
 L29 ANSWER 14 OF 17 MEDLINE  
 AN 84038061 MEDLINE  
 DN 84038061 PubMed ID: 6632936  
 TI Lipids and cholesterol esterifying enzyme changes by Anna Pavala Sindhooram therapy in experimental rat hyperlipaemia.

AU Shanmugasundaram K R; Parthasarathy R  
 SO JOURNAL OF ETHNOPHARMACOLOGY, (1983 Jul) 8 (1) 35-52.  
 Journal code: K8T; 7903310. ISSN: 0378-8741.  
 CY Switzerland  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198312  
 ED Entered STN: 19900319  
 Last Updated on STN: 19900319  
 Entered Medline: 19831220  
 AB The effect of Anna Pavala Sindhooram (APS), an indigenous drug showing lipid lowering action was tested in experimental rat atherosclerosis induced by feeding an atherogenic diet. APS was found to decrease the levels of serum cholesterol and phospholipids while triglycerides remained unaffected in atherogenic diet fed rats. Lipid levels in the aorta, liver and intestine were also increased by atherogenic diet feeding, and APS administration with diet restriction reversed this trend. Cholesterol ester was lowered. Both **cholesterol ester hydrolase** (CEH) and **synthetase** (CES) activities in the tissues were elevated while the CEH/CES ratio was lowered in atherosclerosis. APS administration led to a decrease in enzyme activities and an increase in the CEH/CES ratio. APS *in vitro* inhibited both enzyme activities. NMR spectroscopic studies showed that the soluble components of APS bind or modify cholesterol. Iron, copper, magnesium and calcium present in APS may play a role in the removal of cholesterol ester from the aorta and its disposal.  
 CT Check Tags: Animal; Male; Support, Non-U.S. Gov't  
     \***Antilipemic Agents**: PD, pharmacology  
     Arteriosclerosis: DT, drug therapy  
     \*Arteriosclerosis: ME, metabolism  
     Arteriosclerosis: PA, pathology  
     \*Carboxylic Ester Hydrolases: ME, metabolism  
     \***Cholesterol Esterase**: ME, metabolism  
     Hyperlipidemia: DT, drug therapy  
     Hyperlipidemia: ME, metabolism  
     \*Lipids: ME, metabolism  
     \*Medicine, Ayurvedic  
     Minerals: PD, pharmacology  
     Rats  
     Rats, Inbred Strains  
 L29 ANSWER 15 OF 17 MEDLINE  
 AN 81123984 MEDLINE  
 DN 81123984 PubMed ID: 233431  
 TI Effects of phthalazinol (EG 626) on arterial lipolytic enzyme activities in the rat.  
 AU Tomita T; Yonekura I; Shirasaki Y; Hayashi E; Numano F  
 SO PAROI ARTERIELLE, (1979 Dec) 5 (4) 181-4.  
 Journal code: ORO; 7606268. ISSN: 0398-7655.  
 CY France  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 198104  
 ED Entered STN: 19900316  
 Last Updated on STN: 19900316  
 Entered Medline: 19810413  
 AB Phthalazinol (EG 626), a thromboxane A<sub>2</sub> antagonist and cyclic AMP phosphodiesterase inhibitor, has been shown to prevent the atherosclerosis induced in cholesterol fed rabbits. In an attempt to clarify the antiatherosclerotic mechanism, the effects of this compound on the lipolytic enzyme activities (**cholesterol esterase** and

lipoprotein lipase) of rat aorta were examined in vivo. Administration of EG 626 (100-200 mg/kg, per os, daily, 1-2 weeks) affected neither the aortic lysosomal **cholesterol esterase** nor the acid phosphatase activity, whereas the lipoprotein lipase activity was significantly decreased by the treatment. These results suggest that with an elevation in HDL-cholesterol, a decrease in lipoprotein lipase activity after ingestion of EG 626 might contribute, at least to some extent, to the prevention of arterial lipid accumulation.

CT Check Tags: Animal; Comparative Study; Male  
 3',5'-Cyclic-Nucleotide Phosphodiesterase: AI, antagonists & inhibitors  
 Acid Phosphatase: ME, metabolism  
 Aorta  
 \*Arteries: DE, drug effects  
 Arteries: ME, metabolism  
 Arteriosclerosis: PC, prevention & control  
 Cholesterol: BL, blood  
 Cholesterol Esterase: ME, metabolism  
 \*Lipolysis: DE, drug effects  
 Lipoprotein Lipase: AI, antagonists & inhibitors  
 Lipoproteins, HDL: BL, blood  
 \*Phthalazines: PD, pharmacology  
 \*Pyridazines: PD, pharmacology  
 Rats

L29 ANSWER 16 OF 17 MEDLINE  
 AN 79082488 MEDLINE  
 DN 79082488 PubMed ID: 728232  
 TI Regression of naturally occurring atherosclerotic lesions in pigeon aorta by intestinal bypass surgery. Early changes in arterial cholestryll ester metabolism.  
 AU Ravi Subbiah M T; Dicke B A; Kottke B A; Carlo I A; Dinh D M  
 SO ATHEROSCLEROSIS, (1978 Oct) 31 (2) 117-24.  
 Journal code: 95X; 0242543. ISSN: 0021-9150.  
 CY Netherlands  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals  
 EM 197902  
 ED Entered STN: 19900314  
 Last Updated on STN: 19900314  
 Entered Medline: 19790226  
 AB Early changes in cholestryll ester metabolism of the aorta during the regression of naturally occurring atherosclerotic lesions in pigeon aorta by ileal bypass surgery were examined. Three months after surgery, there was a decrease (50%) in the content of cholestryll esters in the aorta. Increases in the activity of cholestryll ester hydrolase in the lysosomal (P less than 0.05) and the supernatant (P less than 0.01) fractions of the aorta also occurred at this time. There were no differences in the activity of cholestryll ester synthetase and in the plasma levels of cholesterol and triglycerides between the ileal bypass group and the controls. These results suggest that ileal bypass surgery decreases the level of cholestryll esters in the aorta, probably because of enhanced cholestryll ester hydrolysis.  
 CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.  
 \*Aorta: AN, analysis  
 Arteriosclerosis: EN, enzymology  
 \*Arteriosclerosis: SU, surgery  
 Cholesterol Esterase: ME, metabolism  
 \*Cholesterol Esters: AN, analysis  
 \*Intestine, Small: SU, surgery  
 Pigeons

AN 78037400 MEDLINE  
DN 78037400 PubMed ID: 920445  
TI Arterial cholesterol esterase.  
AU Kritchevsky D  
SO ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1977) 82 878-81.  
Journal code: 2LU; 0121103. ISSN: 0065-2598.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals  
EM 197712  
ED Entered STN: 19900314  
Last Updated on STN: 19900314  
Entered Medline: 19771229  
CT Check Tags: Animal; Support, U.S. Gov't, P.H.S.  
\*Antilipemic Agents: PD, pharmacology  
Aorta: EN, enzymology  
\*Aorta: ME, metabolism  
\*Arteriosclerosis: ME, metabolism  
\*Carboxylic Ester Hydrolases: ME, metabolism  
\*Cholesterol Esterase: ME, metabolism  
\*Cholesterol Esters: BI, biosynthesis  
Clofibrate: PD, pharmacology  
Dextrothyroxine: PD, pharmacology  
Dietary Fats  
Nicotinic Acids: PD, pharmacology  
Oils  
Sitosterols: PD, pharmacology